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Eileen F. Terrill

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WOMEN'S EXPERIENCES OF MANAGING
RELAPSING-REMITTING MULTIPLE SCLEROSIS
WITH DISEASE MODIFYING DRUGS

A Dissertation Presented

by

Eileen F. Terrill

Submitted to the Graduate School of the
University of Massachusetts, Worcester, in
partial fulfillment of the requirements for
the degree of

DOCTOR OF PHILOSOPHY

May 2007

Nursing

“Women’s Experiences of Managing Relapsing-Remitting Multiple Sclerosis with
Injectable Disease Modifying Drugs”

A Dissertation Presented

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Dedication

This dissertation is dedicated to my sister-in-law, Marilyn Keyes, whose courage and perseverance inspired me in my work.

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Abstract

Purpose: To describe the experience of managing relapsing-remitting multiple sclerosis among adult women users of injectable disease modifying drugs, including day-to-day management, medication beliefs, and health care provider influence.

Rationale/Significance of the study: Approximately 85% of the 400,000 Americans with multiple sclerosis have relapsing-remitting multiple sclerosis (RRMS), characterized by unpredictable relapses and partial or full remissions of neurological symptoms.

Untreated, RRMS may progress to permanent, irreversible disability and decreased quality of life. Current guidelines recommend immediate and sustained treatment with injectable disease modifying drugs (DMDs). However, despite pronounced modest benefits, approximately 30%-62% of patients are not undergoing DMD therapy. A small number of quantitative studies have identified factors that predict adherence to injectable DMDs. However, little is known about injectable DMDs from patients' perspectives. It is important to develop an understanding of the experience of managing RRMS among adult users of injectable DMDs in order for health care providers to provide ongoing education, counseling, and support.

Organizing Framework: The framework, Beliefs About Medicines, was used to guide the study.

Design: Qualitative descriptive design.

Setting: Data were collected from adult women with RRMS who received care from an MS clinic, a neurology practice, and through snowball sampling.

Sample: Purposive and theoretical sampling was used to recruit 32 women with RRMS. Maximum variation sampling ensured the appropriate breadth and depth of experiences.

Women currently undergoing injectable DMD therapy ($n = 25$), as well as women who either discontinued ($n = 6$), or never used ($n = 1$) injectable DMDs were interviewed.

Methods: A qualitative descriptive design was utilized. Verification occurred through trustworthiness of data, including rich, thick description from qualitative interviews; field notes and memoing; and member checks. Simultaneous data collection, analysis, and interpretation facilitated interview revision in order to elicit or expand emerging themes. Content analysis inductively derived themes and patterns within and across categories. Participant quotes substantiated particular themes. Confirmability of the data analysis process was undertaken in consultation with the research advisor.

Implications: Findings elucidated adult women's subjective experiences concerning management of RRMS among users of DMDs, including day-to-day management, medication beliefs, and health care provider influence. Results from this study can be used to educate, counsel, and support women in the management of RRMS.

Chapter I

Introduction

Approximately 85% of patients diagnosed with multiple sclerosis (MS) experience the relapsing-remitting subtype (Lublin & Reingold, 1996). Close to 300,000 individuals living in the United States with this autoimmune neuroinflammatory illness face periods of transient, unpredictable, and potentially disabling symptomatology, as well as an uncertain illness trajectory (Anderson, et al., 1992). Furthermore, researchers estimate that up to 90% of individuals with relapsing-remitting multiple sclerosis (RRMS) may progress to a more serious and debilitating form of the disease (Weinshenker, et al., 1989a). The unstable nature of RRMS can lead to lost revenues due to increased work absences (Gedizliogu et al., 2000; Kobelt, Berg, Atherly, & Hadjimichael, 2006), an abrupt end to employment (Grima et al., 2000; Kobelt, Berg, Lindgren, Fredrikson, Jonsson, 2006; O'Day, 1998), and increased use of health care resources (Milteneburger & Kobelt, 2002; National Multiple Sclerosis Society, 2002a; Phillips, 2004; Pope, Urato, Kulas, Kronick, & Gilmer, 2002). As a result, the impact of RRMS can be physically, financially, and emotionally devastating, and lead to a poor quality of life (Grima et al., 2000; McCabew & De Judicibus, 2005; Merkelbach, Sittinger, & Koenig, 2002; Parkin, McNamee, Miller, Thomas, & Bates, 2000; Solari & Radice, 2001).

Injectable DMDs (formerly called injectable immune modulators), introduced in the 1990's, have been instrumental in minimizing or eradicating symptoms, lengthening remissions, and retarding the progression of RRMS (Fernandez et al, 2003; Galetta, Markowitz, & Lee, 2002; Jacobs et al, 1996; Johnson et al, 1995; Paty, Li, the UBC

MS/MRI study group, & the IFNB Multiple Sclerosis Study Group, 1998). Although not a cure, the use of injectable DMD therapy has resulted in improved quality of life for some individuals with RRMS (Arnoldus, et al., 2000; Hemmet, et al., 2004; Isaksson, Ahlstrom, & Gunnarsson, 2005; Kobelt, et al, 2006; Lily, McFadden, Hensor, Johnson, & Ford, 2006; Zivadinov et al., 2003). Yet, despite the pronounced benefits of injectable DMD therapy, an estimated 30% (Lo, Hadjimichael, & Vollmer, 2005) to 62% (Avasarala, O'Donovan, Roach, Camacho, & Feldman, 2007) of patients with RRMS are not currently using it. Moreover, several studies have indicated that many patients who are engaged in injectable DMD therapy abandon therapy within the first two years (Munschauer & Tyree, 2004; NARCOMS News, 1999; PharMetrics Patient Centric Database, data on file, 2000-2002; Rio, et al., 2005; Ruggieri, et al, 2003). The most common reasons given for treatment discontinuation are worsening symptoms (Hadjimichael & Vollmer, 1999), perceived lack of drug efficacy (Onesti et al., 2003; O'Rourke & Hutchinson, 2005; Tremlett & Oger, 2003), and treatment side effects (Daugherty, Butler, Mattingly, & Ryan, 2005).

A small number of quantitative studies in the literature measured factors that influence patients' adherence to injectable DMD therapy , including self-efficacy, hope, physician support, previous use of injectable DMDs (Fraser, Hadjimichael, & Vollmer, 2001), mood (Mohr et al., 2000), pretreatment expectations, and post-injection anxiety (Mohr, Boudewyn, Likosky, Levine, & Goodkin, 2001).

A phenomenological study of patients with RRMS ($n = 15$) undergoing treatment (with IFNB-1a) focused on patients' physical, cognitive, and emotional adaptation to the illness and treatment (Miller & Jezewski, 2001). A more recent qualitative study by

Johnson and colleagues (2006) focused on perspectives regarding the injectable DMDs among patients with MS ($n = 18$). Patients who were using injectable DMDs ($n = 11$) described positive (disease stability, feeling of control) and negative (cost of medication, fear, and uncertainty) aspects of treatment. Patients who were not on therapy, including those who discontinued use ($n = 2$) and those who never started ($n = 5$), described reasons for non-use, including fear of needles, lack of active disease, fear of side effects, and cost.

There are several differences between the study by Johnson et al (2006) and this researcher's dissertation study. First, the study sampled 18 participants from a larger pool of volunteers. A small number of the participants had a form of MS other than RRMS (primary progressive, $n = 1$; secondary progressive $n = 1$). Further, the study included men ($n = 2$). In addition, perspectives about 'opting out' of treatment were recorded from all non-users of injectable DMDs, making it difficult to distinguish perspectives of those who had discontinued use from those who had never used the medication. Finally, the study only studied perspectives related to use or non-use of injectable DMDs. Little detail is available about patients' subjective experiences of managing RRMS among users and nonusers of injectable DMDs, including day-to-day management, barriers to treatment, personal medication beliefs, and the influence of health care providers. Therefore, the purpose of this qualitative descriptive study was to develop a clear understanding of the experience of managing RRMS among adult women users and nonusers of injectable DMD therapy.

The specific aims of the proposed research were to:

- 1) Describe the subjective experience of the day-to-day management of RRMS among adult women who were currently using injectable DMDs, had never used injectable DMD, or had stopped using injectable DMDs.
- 2) Examine treatment beliefs, including treatment necessity and perceived concerns, related to injectable DMD therapy among patients with RRMS who were using or not using injectable DMD therapy.
- 3) Examine the influence of health care providers on treatment beliefs and management of injectable DMD therapy among adult patients with RRMS who were using or not using injectable DMD therapy.

Background and Significance

Incidence and Prevalence

Multiple sclerosis (MS) is a chronic neuroinflammatory disease that affects most individuals between the ages of 15 and 45 (Jacobson, Gange, Rose, & Graham, 1997). Approximately 1.5 million individuals worldwide live with MS, and, in the United States, more than 400,000 cases have been identified (National Multiple Sclerosis Society, 2004a). Each year an estimated 8,500 to 10,000 new cases are diagnosed (Jacobson et al., 1997). MS is more prevalent among Caucasians, and women are more than twice as likely to be affected as men (Anderson et al, 1992).

The cause of MS is unknown, although several theories continue to be explored, including genetics (Ebers & Sadovnick, 1994; Prat & Martin, 2002; Ransohoff, 2000), environment (Kurtzke, 1988; Pugliati, Sotgiu, & Rosati, 2002), infectious agents (Cook & Dowling, 1980; Kurtzke, 1993) and biochemical factors (Casetta & Granieri, 2000;

Kurtzke, 1993; Noseworthy, Lucchinetti, Rodriguez, & Weinshenker, 2000). At the present time, there is no known cure for MS. Although MS does not shorten an adult's lifespan, its disabling nature can affect quality of life for many individuals. It is the third most common neurological cause of disability among young people (ages 20-40) (Salan, 2003).

Relapsing Form of MS

MS is now believed to be a heterogeneous disease, with diverse pathological processes and clinical presentations occurring among and within persons at any given time (Galetta, Markowitz, & Lee, 2002; Lucchinetti et al., 2000; Ransohoff, 2000; Weinshenker et al., 1989b). Four subtypes of MS have been distinguished: relapsing-remitting, primary progressive, secondary-progressive, and relapsing-progressive MS (see Table 1 for a description; Lublin & Reingold, 1996). Approximately 85% of persons with MS have the relapsing-remitting subtype (RRMS). Researchers have suggested that relapsing-remitting MS (RRMS) and secondary-progressive MS (SPMS) are part of the same continuum of active disease progression (Ransohoff, 2000). In particular, Weinshenker and colleagues (1989a) found further evidence in this regard, as 50% of individuals with untreated RRMS advance to SPMS within 10 years, and 90% advance within 25 years.

The hallmarks of RRMS are intermittent, acutely inflammatory neurological attacks (relapses) followed by periods of either partial or complete recovery (remissions) (Lublin & Reingold, 1996; Weinshenker et al., 1989b). Relapses occur unexpectedly and gradually (Phillips, 2004), typically lasting longer than 24 hours (Schumacher et al., 1965). Over the course of a relapse, individuals may experience such symptoms as

blurred vision, pain, extreme fatigue, muscle spasticity or weakness, varying degrees of urine or fecal incontinence, ataxia, or cognitive impairment (Paty, 2000). A remission may occur over weeks to months (Phillips, 2004; The IFNB Multiple Sclerosis Study Group, 1993).

The clinical course of RRMS is unpredictable and different for each individual, making diagnosis and treatment difficult. Early in RRMS, the average rate of relapses is approximately one per year (range 0.1 to 1.0; Compston & Coles, 2002). As the disease progresses, the relapses may subside, and individuals may experience a slow but gradual decline (Confavreux et al., 2000; Lacey et al., 2000). In a study of 190 patients with RRMS, Amato and Ponziani (2000) found that residual disability post-relapse was a more important predictor of secondary progression ($p < .0001$) than the number of relapses (in the first 2 years). Kurtzke developed the Expanded Disability Status Scale (EDSS) (1983) which is used widely to measure the progression of MS and to evaluate treatment efficacy (See Table 2). Confavreux and colleagues (2000) used the EDSS to determine the timeline of progression from RRMS to SPMS, charting a median time of 15 years to use of a cane (EDSS 6), 20 years to wheelchair use (EDSS 7), and 25 years to full confinement to wheelchair or bed (EDSS 8).

Pathophysiology of RRMS

The mechanism of neurological damage in RRMS is complex and not well understood. Some scientists purport that two main pathological processes, myelin sheath destruction and nerve fiber (axonal) damage, occur concomitantly (Smith & McDonald, 1999). An unknown event triggers an autoimmune process of inflammation and demyelination of the myelin sheath in the brain and spinal column (Trapp et al., 1998).

The myelin sheath, a fatty, white, protective covering of the neurons, normally facilitates the transmission of nervous impulses. With demyelination, lesions or plaques disrupt the surface of the myelin sheath, while inflammatory by-products damage the underlying axon (Comi, 2000; Ransohoff, 2000, Trapp et al., 1998). The nerve impulses become erratic, transient, and slowed, which may result in neurological signs or symptoms (Ransohoff, 2000; Trapp, Ransohoff, & Rudick, 1999). Subsequently, as the inflammation resolves and partial remyelination restores conduction, neurological symptoms tend to decrease or disappear (Smith & McDonald, 1999). This destructive process begins early in the disease and may be present without manifestation of clinical signs or symptoms (Comi, 2000; Coyle, 2003).

The relevance of axonal damage in the course of RRMS is not yet fully understood, and has been under debate. Some researchers have suggested that axonal damage occurs as a result of the early and persistent inflammation in relapses (Miller, Grossman, Reingold, & McFarland, 1999; Ransohoff, 2000; Trapp, et al., 1998). The early subclinical axonal damage appears to continue even after the inflammation resolves (Confavreux et al., 2000; Komek & Lassman, 2000), and may result in brain atrophy (evident on MRI) (Ransohoff, 2000). However, Chaudhuri and Behan (2005) argued that the inflammatory event and axonal damage are unrelated, and have cast doubt on the efficacy of the current injectable DMD therapy. They proposed that the axonal damage causes degeneration that is not halted by the immunologic properties of the injectable DMDs.

Psychosocial impact of RRMS

The average age of onset of RRMS is 30 (Confavreaux et al., 2000). Therefore, this disease can have financial, vocational, and social implications for young people during their most productive years. One survey of 246 individuals found that the greatest impact of RRMS was on reduction of income (37%), unemployment (40%), change in hobby (25%), social isolation (29%) and increased need for assistance (37%) (Gedizliogu et al., 2000). Moreover, 60% of the \$20 billion annual cost related to MS in the United States (National Multiple Sclerosis Society, 2004a) is attributed to lost productivity and caregiving by the family (Grima et al., 2000; Miltenberger & Kobelt, 2002; Kobelt, et al, 2006).

The unpredictable nature of relapses, short-lived yet bothersome symptoms, and varying degrees of disability inherent in RRMS may cause individuals to make changes in their work habits (Smith & Arnett, 2005; Solari & Radice, 2001). Earlier studies indicated that approximately 70 to 80 per cent of individuals with MS stopped working within five years of diagnosis (O'Day, 1998). However, more recently, Smith and Arnett (2005) found that some individuals decide to continue to work, though in a lesser capacity. Johnson and colleagues (2004) suggested that a combination of personal, functional, and workplace limitations cause reduced employment for many patients with RRMS. For example, Smith and Arnett (2005) reported that 90% of workers cut back their work due to fatigue. Conversely, factors such as advanced education, desirable job, insurance needs, and mild symptoms may impact the decision to continue working part-time.

Studies indicated that employment among individuals with MS decreases as the level of disability (EDSS) increases (Grima et al., 2000; Smith & Arnett, 2005). In one study, full time employment decreased from 51% at EDSS 1 to 5% at EDSS 6 (Gedizlioglu et al, 2000). Absences caused by increasing disability or relapses may range from 73-87% (Grima et al., 2000). Other consequences of the disease include time lost from work (Gedizlioglu et al., 2000; Grima et al., 2000), job change or revision (Gedizlioglu et al., 2000), loss of social and professional contacts (Hakim, 2000), and early retirement (Grima et al., 2000; O'Day, 1998). The loss of employment and reduced or lost wages may result in a decreased quality of life for many patients and their families (Grima et al., 2000; McCabew & De Judicibus, 2005; Merkelbach, et al., 2002; Parkin, et al., 2000; Solari & Radice, 2001).

Pope and colleagues (2002) found that health care utilization among insured individuals with MS (private insurance, Medicare, Medicaid) is two to three times higher than individuals without MS. Health care costs related to RRMS include increased use of health care commensurate with increased disability (increased EDSS) and intermittent relapses (Grima et al., 2000; Miltenburger & Kobelt, 2002; Phillips, 2004). The cost of a relapse can range from \$248 for mild relapses to \$12,870 for severe relapses (O'Brien, Ward, Patrick, & Caro, 2003). These factors, coupled with reduced or lost wages, can have an adverse financial effect on both the patient and their family.

In summary, RRMS is a complex, unpredictable disease with an uncertain illness course. The transient nature of relapses and disability may adversely affect patients' physical, vocational, and social wellbeing. Patients and families may face loss of employment and social contacts, increased health care costs, and a reduced quality of life.

Untreated, the disease may progress to almost total dependency for 90% of patients. However, scientists and researchers continue to make new discoveries regarding the disease, including treatments that alter the immune response (injectable DMDs). Early and sustained injectable DMD therapy may stabilize RRMS, delay progression, reduce healthcare costs and improve quality of life for patients (Flachenecker & Rieckmann, 2003).

Injectable DMDs for RRMS

Injectable DMDs are currently the standard platform therapy for RRMS. Developed in the mid-to-late 1990's, this therapy includes interferon and non-interferon medications. Injectable interferons have been approved by the Food and Drug Administration (FDA) for their anti-inflammatory, immunomodulatory, and antiviral properties (Dhib-Jalbut, 2003; Kendrick & Johnson, 2000). The injectable interferons include Interferon beta-1b (IFNB-1b; Betaseron ©; Berlex Laboratories), Interferon beta-1a intramuscular (IFNB-1a IM; Avonex ©; Biogen, Inc.), and Interferon beta-1a subcutaneous (IFNB-1a SC; Rebif ©; Serono, Inc.). Glatiramer acetate (GA; Copaxone ©; Teva Neuroscience) is a non-interferon synthetic protein medication that blocks the autoimmune inflammatory mechanism in the brain (See Table 3 for a description of the injectable DMDs).

Some uncertainty exists regarding the efficacy of the injectable DMDs. The results of the original two-year, phase III, randomized placebo-controlled clinical trials indicated that both the interferon (IFNB beta-1a IM, IFNB beta-1a SC, IFNB beta-1b) and the non-interferon (glatiramer acetate) medications achieved several outcomes: reduction in the frequency of relapses by approximately 30% (Jacobs et al., 1996;

Johnson et al., 1995; The PRISMS Study Group, 1998; The IFNB Multiple Sclerosis Study Group, 1993), prolonged periods of remission (Johnson et al., 1995; The IFNB Multiple Sclerosis Study Group, 1993), reduction of disease activity, as seen on MRI (Jacobs et al., 1996; Johnson et al., 1995; PRISMS Study Group, 1998; Paty, Li, & The IFNB Multiple Sclerosis Study Group, 1993) and delayed progression of disease, as measured by the EDSS (Jacobs et al., 1996; PRISMS Study Group, 1998). (See Table 4 for efficacy profiles of the immunomodulators). These findings were replicated in extended studies, including the IFNB Multiple Sclerosis Study Group & the University of British Columbia MS/MRI Analysis Group (1995); Johnson et al., (1998); Johnson et al., (2000); The Prisms Study Group, and the University of British Columbia MS/MRI Analysis Group (2001); Panitch et al., (2002); Fernandez, et al., (2003); Onesti et al., (2003); Clanet, Kappos, Hartung, Hohlfeld, and the European IFNB-1a Dose Comparison Study Investigators (2004); and Ford, et al., (2006). However, the validity of these findings has since been debated (Chaudhuri & Behan, 2005; Clanet & Cucherat, 2003; Confavreux et al, 2000; Fillippini et al, 2000; Freedman, King, Oger, Sharief, & Hartung, 2003; Goodin, 2003; Kappos & Kesselring, 2003; Kolar, Baurie, & Lee, 2003; Paty, Arnason, Li, & Traboulsee, 2003; Rice et al., 2001; Rudick, Cookfair, Griffin, Hauser, & Plantadosi, 2003; Greenstein, 2001, 2002). A meta-analysis of the original clinical trials reported that the use of the injectable interferons demonstrated only one outcome: a reduction in the number of patients having relapses (Fillippini et al, 2003). Moreover, this outcome could not be projected beyond one year. The authors attributed their findings to flawed study designs in the original clinical trials.

The meta-analysis was challenged by many of the authors of the original clinical trials (Freedman, et al., 2003; Goodin, 2003; Kappos & Kesselring, 2003; Kolar, et al., 2003; Paty, et al., 2003; Rudick, et al., 2003). As a result, a more comprehensive meta-analysis was conducted by Rice and colleagues (2001), which found that, in addition to the reduced number of patients with relapses, there was also a reduction in the number of participants whose MS had progressed at the end of two years of treatment with interferons (versus patients not on treatment). Munari, Lovati, and Boiko (2004) conducted a similar meta-analysis on the non-interferon, glatiramer acetate, and found a lack of any significant benefits of the medication. More recently, Chaudhuri & Behan (2005) argued that MS is a neurodegenerative, rather than an inflammatory disease; they suggested that the anti-inflammatory properties of the injectable DMDs are ineffective in addressing disease progression.

In summary, current findings suggest that the interferons have a modest benefit in reducing relapses and delaying short-term progression, but long-term efficacy is uncertain (Confavreux et al., 2000). Yet, despite their limited benefits, the injectable DMDs have increased optimism and improved quality of life for many patients with RRMS. Given the early, subclinical, and potentially irreversible neurological damage in RRMS, scientists and clinicians have strongly advocated for injectable DMDs as the most appropriate initial treatment option for all patients diagnosed with RRMS (Comi, 2000; Coyle & Hartung, 2002; Freedman et al., 2002). A consensus statement published by the Medical Advisory Board of the National Multiple Sclerosis Society recommends immediate and prolonged treatment for newly diagnosed cases of RRMS (See Table 5; National Multiple Sclerosis Society, 2005).

Patient response to disease and treatment

Patients with RRMS report a lower quality of life compared to patients with other diseases, as well as the general population. In one study, patients scored lower on every domain in the Medical Outcomes Study Short Form-36 scale (MOS SF-36) compared to patients with Parkinson's disease and healthy controls (except for mental health; Riazi et al., 2003). The MOS-SF 36 is a 36-item self-report instrument that measures patients' health status across 8 domains: physical functioning, role-physical, bodily pain, general health, vitality (energy and fatigue), social function, role-emotional, and mental health (Ware & Shelbourne, 1992). Increasing disability was associated with lower scores on the MOS-SF36 in another study (Prosser, Kuntz, Bar-Or, & Weinstein, 2003). However, a lower quality of life may also be reported by patients with milder impairments (Ford, Gerry, Johnson, & Tennant, 2001). Hemmet, Holmes, Barnes, and Russell (2004) found that patients experiencing a relapse were more likely to report a lower quality of life. McCabe and McKern (2002) found lower subjective and objective measures of all domains of the World Health Organization Quality of Life-100 scale (WHOQOL-100) among patients with RRMS than among the general population. Factors that predict quality of life among patients with RRMS include physical disability, disease progression, fatigue, cognition, and depression (Benedict et al., 2005).

Several studies have examined quality of life among patients with RRMS who are undergoing injectable DMD treatment (Arnoldus, et al., 2000; Gottberg, Gardulf, & Fredrikson, 2000; Hemmet et al., 2004; Isaksson, Ahlstrom, & Gunnarsson, 2005; Lily et al., 2006; Zivadinov et al., 2003). Hemmet and colleagues (2004) found that mean scores on 7 of the 8 domains of the SF-36 were significantly higher among patients ($N = 131$)

who were undergoing beta interferon therapy (type not specified) than among patients ($N = 1554$) who were not on the therapy ($p = <.05$; *physical functioning* domain was $p = .061$). Conversely, Isaksson and colleagues (2005) found no significant difference in MOS SF-36 scores between treated patients.

In spite of their benefits, side effects of the injectable DMDs can affect quality of life for many patients. Arnoldus and colleagues (2000) found a significant increase in one of eight domains (role-functioning scores) on the MOS SF-36 among patients with RRMS during the first six months of treatment with IFNB-1b ($p < .001$). However, patients who reported more side effects were more likely to have lower scores on several subscales, including role-functioning scores, than those who reported fewer side effects. In another study of IFNB-1a (IM) ($n = 17$) and IFNB-1b ($n = 23$), two side effects, asthenia and fatigue, were associated with a lower quality of life (Gottberg et al., 2000). Other studies found no association between self-reported side effects and quality of life during a year of treatment with IFNB-1a (IM) (Vermersch, de Seze, Delisse, Lemaire, & Stojkovic, 2002; Zivadinov et al, 2003).

McGuiness and colleagues (2001) conducted a pilot study among 63 participants who were using either injectable interferons (IFNB-1a, IFNB-1b, or IFNB-1a SC, not specified) or glatiramer acetate. The study measured participants' self-report of post-injection perceived wellness. Those patients using an injectable interferon were 5 times more likely to feel unwell 12-16 hours post injection than the patients who used glatiramer acetate (McGuiness, Lagendyk, Halle, Jacques, & Metz, 2001). Moreover, participants were nearly twice as likely to alter their daily activities because of the side

effects. No details were provided regarding the type or dose of medication, or specific side effects.

In summary, many patients with RRMS report a lower quality of life concerning their physical, cognitive and psychological function. In contrast, patients who are undergoing DMD treatment report an improved quality of life. However, treatment side effects may result in reports of reduced quality of life and disruption in daily living. These factors may influence patients' attitudes and behavior regarding their injectable DMD therapy.

Literature Review

Management of the Injectable DMD

In chronic illnesses such as RRMS, effective disease management may be as critical to patients' wellbeing as their access to health care (Horne, 2003). People with RRMS must somehow incorporate the disease into their lives. In so doing, they must develop a regimen of day-to-day management that includes health care visits and treatment regimens. On average, patients with chronic illness see their health care provider one hour per year, spread over four visits (Kaptein et al., 2003). Therefore, for the most part, patients manage their day-to-day illness on their own.

Patients with chronic illnesses are taking a more active role in treatment planning (Bodenheimer, Lorig, Holman, & Grumbach, 2002; Heesen, Kasper, Segal, Kopke, & Mulhauser, 2004; Nicholl, 2002). This includes deciding whether, when, and how to engage in their therapy. With regard to RRMS, researchers have advocated for immediate and long-term injectable DMD therapy to reduce relapses, delay progression, and improve quality of life. Yet, it is unclear why some patients have successfully initiated

and continued injectable DMD, while others have delayed, interrupted, or discontinued treatment. Many factors influence effective day-to-day management of RRMS with DMDs (Johnson et al., 2006; Nicholl, 2002). Among the most common factors are adherence behaviors, medication adverse effects, financial constraints, injection issues, treatment beliefs, and health care provider influence. Some of these factors may be unnecessary barriers that prohibit effective day-to-day management of the injectable DMDs.

Initiation and Adherence to Injectable DMDs

Recent surveys have revealed that, despite the current treatment recommendations, an estimated one-third to two-thirds of all eligible individuals with RRMS are not using DMDs (Anasarala et al., 2007; Lo, et al., 2005; Miller, Crayton, & Namey, 2004; Taylor & Leitman, 2001). A Harris Interactive Poll conducted in 2001 indicated that 42% of patients with MS were not undergoing the recommended injectable DMD therapy; furthermore, those persons who were 5 years (or longer) from diagnosis were even less likely to be taking the medications (Taylor & Leitman, 2001). However, this could be due to the fact that most of the DMDs were approved for use in the mid-to-late 1990's. Forty-three per cent of those surveyed responded that they were not on the therapy because they were not experiencing active MS disease symptoms. Conversely, Rio and colleagues (2005) found that patients with RRMS who discontinued interferon therapy were young, female, and more disabled than their counterparts at initiation of treatment ($p = <.0001$). A more recent study suggested that non-usage may be as high at 62% among patients treated by a neurologist, and 92% by patients seen by family

practitioners or internists (Anasarala et al., 2007). There was no indication of the reason for non-usage in the study.

Other reported reasons for not being on the medication have been related to medication effects, patients' beliefs, cost, and health care provider influence. Daugherty and colleagues (2005) found that discontinuation of injectable DMDs was based on adverse effects, disease progression, perceived lack of efficacy, and cost. Similarly, Johnson and colleagues reported that patients with RRMS stopped injectable DMD therapy due to concerns regarding side effects, feeling well, fear of needles, cost, and physician recommendation (Johnson, et al., 2006). In both studies, type of injectable DMD was not a factor.

Length of time on therapy appears to influence adherence. A review of pharmaceutical records of over 21,000 patients who were using injectable DMDs from January 2000 to March 2002 revealed that adherence initially was 68-76% (PharMetrics Patient Centric Database, 2000-2002, data on file). After 2 years on therapy, however, the number of patients continuing the medication decreased by as much as 18%, depending on the injectable DMD. Similarly, Ruggeri and colleagues (2003) found that approximately 50% of nonadherent patients discontinued treatment within the first two years. Munschauer and Tyry (2004) found that 6-11% of patients ($n = 6211$) discontinued injectable DMDs within 6 months of initiation.

Tremlett and Oger (2003) conducted a retrospective chart review of 846 patients who received injectable DMDs over 29 months. One third of the patients stopped treatment for at least one month, and 13 % switched to another treatment. Perceived lack of efficacy, the main reason for stopping or switching, was significantly related to the

type of therapy ($p = <.05$). In another study, particular injectable DMDs were reported to be more problematic than others; for example, of patients who stopped treatment due to perceived progression, 35% were on IFNB-1a IM (Avonex ©), 25% were on glatiramer acetate (Copaxone ©), and 21% were taking IFNB-1b (Betaseron ©) (NARCOMS News, 1999). Ruggieri and colleagues (2003) also found that discontinuation was varied depending on the injectable DMD used.

Several quantitative studies have examined factors that influence adherence to the DMDs. Fraser and colleagues (2001) identified predictors of adherence among patients with RRMS undergoing treatment with glatiramer acetate ($n = 274$), and those who discontinued treatment ($n = 116$). Findings indicated that hope ($p = <.05$), self-efficacy ($p = <.01$), no prior use of immunomodulators ($p = <.03$), and perception of physician support ($p = <.05$) positively influenced adherence. Other studies found that pre-treatment expectations, post-injection anxiety (Mohr, Boudewyn, Likosky, Levine, & Goodkin, 2001) and depression (Mohr et al., 2000) negatively affected adherence.

In summary, despite positive (albeit limited) documented effects of injectable DMDs, one-third to two-thirds of all patients with RRMS are not receiving therapy. Some patients never begin therapy; other patients discontinue treatment up to 2 years after initiation. Still others switch therapies. The most common reasons for non-initiation, switching, or discontinuing treatment are side effects, perceived lack of active disease symptoms, perceived lack of efficacy, perceived disease progression, and health care provider recommendation.

Medication Side effects

Side effects related to injectable DMDs, including flu-like symptoms and injection site reactions, are common among patients with RRMS. For example, approximately 3 to 6 hours after injection, up to 75% of patients initially experience a constellation of flu-like symptoms, including headache, fever, myalgia, fatigue, and chills (Walther and Hohlfield, 1999). These effects are mild, and typically subside within 24 hours, but may persist for several weeks (Gottberg et al., 2000). In the original clinical trials, 48% of the participants reported flu-like symptoms, which disappeared after three months (The IFNB MS Study Group, 1993; Jacobs et al., 1996; The PRISMS Study Group, 1998). The incidence of localized skin injection reactions, including pain, erythema, and swelling, can be as high as 90% (Frohman et al., 2004).

The frequency and nature of adverse effects may vary among the injectable DMDs (Gottberg et al., 2000). IFNB-1b SC (Betaseron ©) may cause more intense reactions than the other interferons (Trojano et al., 2003), while side effects related to IFNB-1a IM (Avonex ©) may be more long-lasting (Zivadinov et al., 2003). Side effects can cause premature discontinuance or switching of the injectable DMDs (Daugherty, et al., 2005; O'Rourke & Hutchinson, 2003). Side effects most frequently cited are flu-like symptoms, headache, fatigue, injection site reactions, and depression (Tremlett & Oger, 2003). (See Table 3 for common side effects).

Other neurological effects related to the injectable DMDs, such as increased spasticity (hypertonia), asthenia, and increased fatigue, may mimic symptoms associated with MS, and their persistence may be confused with relapse or worsening disease (Gottberg et al, 2000, Walther & Hohlfield, 1999; Zivadinov et al., 2003). Hypertonia is

listed as a common side effect with both IFNB-1a IM (data on file, Biogen, 2003), and IFNB-1b SC (data on file, Serono, 2004), and has been attributed to the discontinuation or modification of IFNB-1b SC therapy.

Cost of Injectable DMD

The financial aspect of illness management with the injectable DMDs can be an overwhelming problem when initiating or continuing treatment. In a survey of 562 individuals with RRMS who were not receiving treatment, 33% indicated that cost was an obstacle (Taylor & Leitman, 2001). An earlier survey by NARCOMS News (1999) of over 400 individuals with RRMS also found that cost was the third most common reason for discontinuing treatment.

The annual wholesale cost of the injectable DMDs ranges from \$16,000 to over \$20,000 (National Multiple Sclerosis Society, 2005). Therefore, the actual cost to the patient will be even higher. Some state and federal programs assist uninsured and impoverished individuals, but the main burden of cost is undertaken by the patient and family. The coverage of treatment costs by insurance companies is variable and may be restrictive. According to National Multiple Sclerosis Society statistics (2002a), 60%-65% of individuals have private insurance, 20%-25% have Medicare, 5%-10% have Medicaid, and 5%-10% are uninsured. Many private insurance companies provide at least partial coverage, but may impose strict limitations on the type and extent of treatment. As of 2006, Medicare (Part D) covers approximately 70% of costs of the medication (Jacobs Neurological Institute, 2007). Medicaid also imposes conditions on the type of medication, as well as eligibility for treatment coverage.

Still, the personal expense for injectable DMD treatment is considerable. For example, under the anticipated Medicare prescription benefits, a person whose income is more than \$14,500 (for a married couple, the income is \$19,500), can expect to pay approximately \$5,000 out of pocket annually for an average treatment cost (per injectable DMD) of \$20,000 (Simons & King, 2004). This does not take into account other medications that may be needed (for example, antispasmodics, incontinence medications, etc.) or other health care costs. Given the proportion of individuals who reduce their work schedules or retire early, the cost of treatment may be prohibitive. A survey of over 25,000 individuals over age 18 with disabilities found that uninsured adults were four times more likely to be noncompliant because of cost than those with insurance (Kennedy & Erb, 2002).

Injection Issues

The DMDs are currently only available in the injectable form to patients with RRMS. Approximately half of all individuals are expected to have injection problems (Mohr et al., 2001). Medication taking requires patients to learn new skills (Russell, Conn, & Ashbaugh, 2003). Complex preparation and administration using a syringe, as well as painful skin reactions, can be a problem for many patients (Harris et al., 2005/2006; Nicholl, 2002). Some patients are unable to self-inject because of loss of sensation, weakness in their hands and fingers (Holland et al, 2001), poor hand-eye coordination, and tremor (Munschauer & Weinstock-Guttman, 2000). Others experience pre-injection anxiety (Cox & Stone, 2006). A study of 101 patients with RRMS found that 12 % had discontinued treatment in the first six months (Mohr et al., 2001). Treatment discontinuation was significantly related to pre- injection self-efficacy

expectations ($p = < .0001$), post-injection anxiety ($p = < .05$), and injection administrator ($p = < .0001$). Patients who required someone else to administer the injection discontinued the treatment within 6 months.

Medication Beliefs

Beliefs about medications can influence an individual's attitudes and behavior concerning injectable DMDs. Individuals who are faced with the prospect of long-term medication use must weigh the perceived benefits of the therapy against their concerns, which may include medication side effects, disruptions, uncertain efficacy, and financial constraints (Horne, 1999). Perceived benefits and concerns are unique to each patient in their individual life circumstances. Depending on their beliefs, patients may either initiate and continue their medication regimen, or become intentionally non-adherent (Wroe, 2001).

In a phenomenological study conducted by Miller and Jezewski (2001), patients with RRMS reported experiencing a sense of being 'proactive' in undergoing treatment with injectable beta interferon-1a IM. However, other research suggested that patients who are not experiencing MS symptoms are less likely to be on DMDs (Johnson et al., 2006; Miller, et al., 2004; Taylor & Leitman, 2001). In a survey of 562 patients with RRMS, 87% believed that the main objective of therapy should be to slow progression rather than reduce relapses (Taylor & Leitman, 2001). Yet, patients who are not undergoing therapy may be unaware that the damage and disease are ongoing, even when there are no obvious signs or symptoms (Jewell, 2001). Their beliefs may cause them to delay, or even decline, therapy at a time when it would be most beneficial.

Breakthrough symptoms or worsening disease can occur in some patients despite taking injectable DMDs. The clinical indicators of worsening disease include relapses, new or worsening symptoms, change in cognition, and new lesions (on MRI; Bashir et al, 2002). Many factors can contribute to worsening disease, including infections, neutralizing antibodies, treatment inefficacy, or an unknown etiology (Miller et al, 2004). Generally, an infection (e.g., urinary, respiratory) can cause a ‘pseudo’ relapse, and resolving it will usually mitigate the exacerbation (Confavreux, 2002). On the other hand, neutralizing antibodies, the immune system’s reaction to the injectable interferons, cannot be eradicated, and their presence appears to reduce the efficacy of the interferon (Rice, 2003). Neutralizing antibodies may appear as late as 18 months after the start of therapy, and can occur in any patient (Miller et al, 2004). This may be one of the reasons for delayed switching or discontinuing medication.

In light of the insidious neurological damage in RRMS, random occurrence of neutralizing antibodies, and uncertain efficacy of the injectable DMDs, a panel of experts has recently developed a model for identification and aggressive treatment of disease progression (Bashir et al, 2003). Many researchers are now advocating the use of combination therapy, such as steroids, additional DMDs, or other medications in situations of clinically identified worsening disease (Jeffery, 2004; Stuart & Vermersch, 2004). However, patients may be reluctant to add to their medication regimen, and may, instead, decide to discontinue treatment.

Several studies reported an association between perceived lack of efficacy and the discontinuation or switching of therapy (Onesti et al, 2003; O’Rourke & Hutchinson, 2005; Rio et al, 2005; Ruggieri et al., 2003; Tremlett & Oger, 2003). In a retrospective

chart review, perceived lack of efficacy was the primary factor related to early discontinuance of beta interferon-1a treatment (Tremlett and Oger, 2003). On the other hand, O'Rourke and Hutchinson (2005) found that patients who discontinued therapy due to treatment failure had continued treatment over one year longer than patients who discontinued treatment due to adverse effects. Thus, in spite of adverse effects, some patients' beliefs about injectable DMDs will motivate them to continue treatment.

A pilot study examining patients' (with RRMS) concerns ($N = 63$) prior to beginning injectable DMD treatment found that 86% were concerned about the treatment efficacy; however, 81% were also concerned about side effects. Patients' concerns can influence discontinuation of the treatment, especially if obvious symptoms validate their concerns (Lagendyk, et al., 2001). However, patients may mistake side effects from interferon therapy as worsening symptoms (Calabresi, 2002). Therefore, they may discontinue their treatment before identifying the cause or investigating other treatment options.

In summary, beliefs about medications may influence initiation and continuing of treatment. Perceived lack of efficacy or worsening disease can cause patients to discontinue or switch, even without knowing the cause. Conversely, lack of obvious symptoms may cause patients to doubt active disease and, therefore, delay treatment. Patients may have unrealistic expectations about the injectable DMD treatment. Developing a clear understanding of patients' specific beliefs will help health care providers to educate, counsel and support patients regarding injectable DMD treatment.

Health Care Provider Influence

Little is known about the influence health care providers may have on their patients' knowledge and experiences associated with the use of DMDs. Approximately half (57%) of patients with multiple sclerosis are treated by an MS specialist; the remainder is under the care of a general neurologist or primary care provider (Vickery, et al., 1999). Vickery and colleagues (1999) found that patients who are treated by MS specialists are more likely to be using DMDs and less likely to discontinue treatment ($p = < .05$). His findings were consistent with those of Anasarala and colleagues, who found that up to 92% of patients seen by family practitioners or internists were not on treatment. He also found that 62% of patients seen by neurologists were not on treatment. On the other hand, one study revealed that more than 60% of patients who had stopped their therapy were following their health care provider's directive (Hadjimichael & Vollmer, 1999). However, in that study, no distinction was made of the type of health care provider (i.e., neurologist, MS specialist, etc.).

Management of RRMS has improved since DMDs were introduced in the mid-1990's. Injectable DMDs have achieved several outcomes, including reduction of relapses by 30%, a reduction in active disease, and a delay of progression in the short-term. Studies have suggested that patients who delay DMD use are at higher risk for relapses ($p = < .0001$) and disease progression ($p = < .03$) than patients who started therapy immediately after diagnosis (Johnson et al., 2003). In addition, studies have indicated worsening disease among patients who have discontinued injectable DMDs (Milanese et al., 2003; Rio et al., 2005). A consensus statement regarding treatment for

RRMS has recommended implementing immediate and sustained injectable DMD therapy to take full advantage of the medication's benefits.

Like their patients, eighty-one percent of health care providers perceive the main objective of injectable DMD therapy is to delay progression (Taylor & Leitman, 2001). However, many health care providers may believe their patients are experiencing a benign course, and therefore may advise delaying treatment (Holland et al., 2001; Pittock et al., 2006). A 20-year follow-up study by Pittock and colleagues (2004) found that patients with minimal disability (EDSS of 2 or less) 10 or more years after diagnosis have a 90% chance of remaining stable. This finding, which affects approximately one in five patients, may have implications for decision-making among health care providers and patients. Patients may decide to delay treatment, deciding, with their health care providers, to take a 'watch and wait' approach (Pittock et al., 2004; Pittock et al., 2006).

The decision to delay treatment has been challenged by other researchers, who argued that the predictive certainty of the disease course is low in the first 5 years (Frohman, et al., 2006; Roach, 2006). They further asserted that injectable DMDs are largely ineffective in the progressive phase of MS. They suggested that an evaluation of MS stability using only the EDSS is not sufficient. A more multidimensional assessment should be included to determine disease impact, including quality of life, loss of employment, cognitive impairment, and mood disturbance.

Given the uncertain and unpredictable course of RRMS, health care provider influence may be an important factor in patients' experiences with management of injectable DMDs (Thorne, Con, McGuinness, McPherson, & Harris, 2004). Fraser and colleagues (2001) reported that health care provider support was a predictor of adherence

to injectable DMDs among patients with RRMS ($p = <.05$). Yet, no description of the type of support was available from the study. Moreover, little information is available about the patient-provider decision-making process concerning initiating or continuing injectable DMD treatment. Zwibel (2003) found that, in the decision-making process concerning initiation of injectable DMDs, patients with RRMS and their physicians collaborated only 56% of the time, while patients alone made decisions 40% of the time. Moreover, some patients terminate their injectable DMD therapy between health care visits without informing their health care provider (Stickel, 2005). Patients and health care providers may have different perspectives on beliefs, concerns, adherence, and quality of life issues related to the treatment. Insight into patients' daily experiences, including perceived barriers to treatment, beliefs, and concerns, may aid health care providers in providing appropriate support for day-to-day management.

Nurses are important participants in the team of health professionals that provides comprehensive care for patients with RRMS. Nurses may coordinate education, counseling, and support services for these patients. Many nursing organizations have derived guidelines and consensus documents regarding medication management and adherence issues related to DMD (Costello, Halper, Harris, & Kennedy, 2003; Denis et al., 2004; Holland et al., 2001a, 2001b). While these recommendations are based on quantitative studies and clinical anecdotes, the unique perspective of the patient with RRMS is largely absent. A qualitative description of the patients' experience will provide important insights into the factors that influence effective management of injectable DMDs. That information will allow nurses and other health care providers to construct interventions that target these factors and improve management of the injectable DMDs.

Chapter II

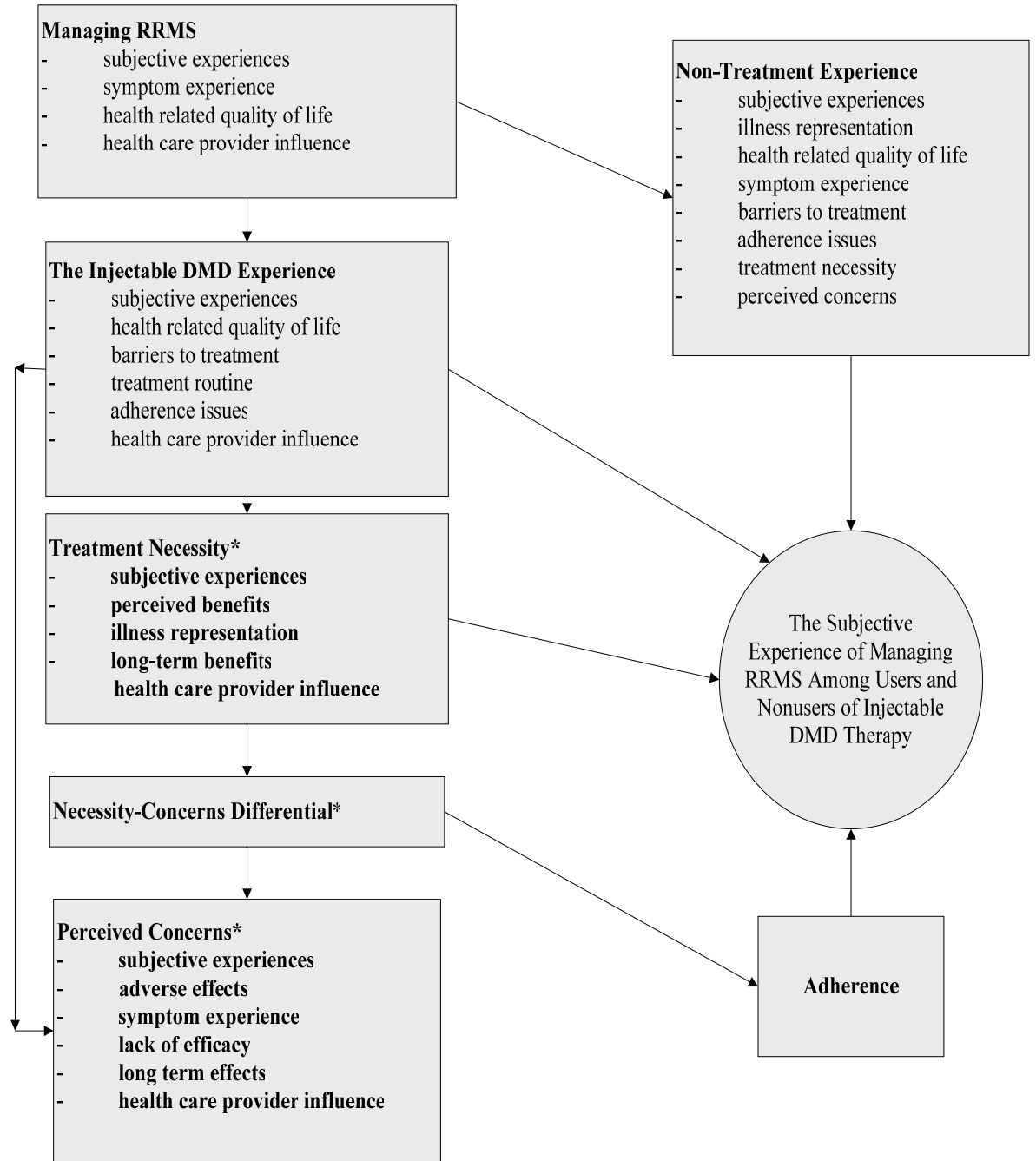
Conceptual Framework

The organizing framework, *Beliefs About Medicines* (Horne, 1997), guided this qualitative study of the experience of managing RRMS among users and nonusers of injectable DMDs (see Figure 1). The framework purports that people's adherence behaviors concerning medications are influenced by their beliefs. Individuals' beliefs arise from their experience (current and prior) with medications or their interpretation of acquired information. According to the Beliefs About Medicines framework, patients participate in a continual process of weighing perceived needs for the medication (e.g, to improve or maintain health) against concerns regarding the medication's effect on day-to-day living (Horne & Weinman, 2002). The appraisal process is continuous, and the outcome (adherence behavior) may change depending on changing beliefs.

Effective medication management requires ability and motivation (Horne, 2003). People's ability to take medications may be affected by obstacles such as inconvenience, disruption, finances, lack of understanding, forgetfulness, or physical impairment. Yet, despite perceived barriers, many patients are adherent to their medication regimen. Prior medication adherence studies focused on the patients' abilities to take medications, for example, comprehending, following directions, and remembering to take medications (Haynes, McKibbin, & Kanani, 1996; Horne, 1998; Wroe, 2001). However, little is understood about the role of motivation in adherence to medication regimens.

Understanding what motivates individuals to begin a difficult medication regimen may help health care providers to better counsel, educate and support their patients (Horne, 1999).

Figure 1. Organizing Framework for the Study of Patients' Experiences with Injectable DMD Treatment.



Bolded text represents concepts from the Beliefs About Medicines Framework.

Source: Horne, R. (1997). Representations of medication and treatment: Advances in theory and measurement. In K.J. Petrie & J. A. Weinman, *Perceptions of health & illness*. The Netherlands: Harwood Academic Publishers, 155-188.

Development of the Framework

The Beliefs About Medicines framework is congruent with social cognitive models (SCM), whose focus is on health-related behaviors. Two SCMs in particular, the Health Belief Model (HBM) (Rosenstock, 1974), and the Theory of Reasoned Action (TRA) (Ajzen & Fishbein, 1980), have been used to explain preventive health and adherence to medications. These models attempt to predict individuals' health-related behaviors in terms of their beliefs, expectations, and values. For instance, the Health Belief Model suggests that patients evaluate their medication regimen based on several factors: the perceived threat of the illness and its consequences, the value that they place on the treatment, and their expected outcomes. The Theory of Reasoned Action proposes that intention and attitude (based on beliefs, normative values, and expectations) are predictive of adherence.

The Beliefs About Medicines framework differs from these models in several ways. First, the Beliefs About Medicines framework evaluates not only the process of forming beliefs, but also examines the content of those beliefs (Horne, 2003). Second, the Beliefs About Medicines framework suggests that health beliefs and behaviors are formed by continual appraisal of the medication and adherence outcomes. The Health Belief Model and Theory of Reasoned action purport that adherence is the result of a single decision. Moreover, the Theory of Reasoned Action is generally applied in circumstances where the patient believes they have control over the situation. Medication taking is often prescribed in circumstances that are out of patients' control. Finally, the Health Belief Model and Theory of Reasoned Action assert that health behavior is driven by external motivation (e.g., health care providers, normative beliefs), while the Beliefs

About Medicines framework explores patients' internal motivations (beliefs). The dynamic interaction of appraisal, belief formations, and adherence behaviors related to medications makes the Beliefs About Medicines framework the most appropriate organizing framework for this qualitative descriptive study.

Conceptual Meanings

The Beliefs About Medicines framework is composed of five constructs: General-Harm, General-Overuse, Treatment Necessity, Perceived Concerns and Necessity-Concerns Differential. General Harm and General-Overuse refer to patients' perceptions about medicines in general. In order to focus on beliefs about particular medicines, only the related constructs, *Treatment Necessity*, *Perceived Concerns* and *Necessity-Concerns Differential*, will be explained in this study (See Table 7).

Assumptions of the Beliefs About Medications Theory

- 1) Patients' adherence to their medication regimen are influenced by their beliefs about the medicine.
- 2) Patients generate a set of beliefs about their prescribed medicine, including perceived treatment necessity and specific concerns; a predominance of one set of beliefs over the other determines adherence behaviors.
- 3) Patients' treatment beliefs are influenced by beliefs they hold about their illness, information or experiences related to the prescribed medicine, and perceptions of personal identity and control.
- 4) Patients maintain a constant appraisal of their adherence behavior concerning their medication regimen; the appraisal may lead to a reinforcement or change in treatment beliefs.

Characteristics of the Beliefs About Medicines Framework

Treatment Necessity

Treatment necessity is the belief that a particular medication is essential for treatment. Perceived need is individual and may be influenced by several factors, including beliefs about medicines in general, prior experience with the medication, illness beliefs, filtered information, and social or cultural expectations (Carder, Vuckovic, & Green, 2003). Beliefs about the medication concern its identity, cause, timeline, cure/controllability, and consequences (Horne et al, 2003). Information about the medication may be acquired from various sources, including the social network, written materials, online resources, or health care providers. Perceived need can change according to changing information, experiences, or beliefs.

Perceived treatment necessity is related to patients' perceptions of their illness (Horne & Weinman, 2002; Vaughan, Morrison, & Miller, 2003). Initially, many patients assess their illness to determine whether it warrants treatment (medication). Patients may view their illness as temporary, and believe they can 'ride out' their condition without medication. The onset, duration, and intensity of the condition can also influence their decision. For instance, acute, persistent, or bothersome symptoms may provoke the desire for palliative or prophylactic medication; conversely, unpredictable, sporadic, or mild symptoms may convince patients that the illness is benign and doesn't require medication (Horne et al, 2001b). The long-term consequences of the illness may influence patients' decisions to start a medication regimen. Patients may fear the long term prognosis of disability, and see the medication as a way to ward off problems. For example, people who believed that asthma would last a long time with severe consequences had stronger

beliefs in the necessity of their prescribed medication and reported lower personal nonadherence (Horne & Weinman, 2002).

Perceived treatment necessity is also related to the person's sense of identity and control. After diagnosis, many patients want to maintain their sense of the 'old self', even as they redefine themselves as medication takers (Carder et al., 2003). For asymptomatic patients, taking the medication may be the only sign of the disease. They may decline medication because of the fear that they may become different. However, the need to take medication may also signify the need for self-efficacy or control over the disease. Other patients perceive themselves to be immune to illness. A study of 100 HIV-positive patients found that perceptions of invulnerability to disease were related to refusal of antiretroviral medications (Cooper et al, 2002).

Specific concerns

Patients' perceived needs concerning their medication are countered by their concerns regarding its negative effects. *Specific concerns* are anticipations of unpleasant adverse effects or disruption by a particular medication. Concerns may develop from concrete experiences with the medication (i.e., adverse effects, disruption). Concerns may also be based on misinformation or miscommunication between the health care provider and patient (Horne, 1997). Other worries include the long term effects of the medication on the body. This set of concerns is universal across medication regimens.

Concerns about adverse effects, disruption, or lack of efficacy may cause patients to delay or discontinue their medication regimen. For example, new or worsening symptoms may signify lack of efficacy (Jopson & Ross-Morris, 2003). Therefore, patients may decide to "take a chance" and forgo treatment rather than utilize a

medication that they perceive is ineffective, inconvenient, and unpleasant. For some patients, non-adherence could be a deliberate attempt to avoid or minimize harmful effects; for other patients, doubts about medication efficacy may cause them to forget to take their dose. (Horne, 2003).

Necessity-concern differential

The *necessity-concern differential* is described as a balance between perceived need and specific concerns about a medication. When initiating or continuing a medication, many patients conduct a general “cost-benefit” appraisal, along with an examination of their personal beliefs and expectations. This cost-benefit assessment may vary both among and within individuals at different times. In general, however, the necessity-concern differential may predict patients’ attitudes and behaviors (adherence) toward the medication. Strong perceptions of personal need may override concerns about the adverse effects (Horne, 1997). On the other hand, moderate levels of concern might stimulate avoidance of the medication, if necessity beliefs are low. This is particularly true if the person has little manifestation of the illness, and the adverse effects of the medication are disruptive and bothersome. In some studies, lower adherence was associated with a higher level of concern (versus perceived need) (Horne, 1997). In contrast, treatment necessity that outweighed specific concerns was related to greater adherence. Patients may also be partially adherent in some circumstances (Carder et al, 2003).

Use of the Theory in Research

The Beliefs About Medicines framework has been used to study adherence in patients with asthma (Chambers, Markson, Diamond, Lasch, & Berger, 1999; Horne &

Weinman, 2002), chronic illnesses (Horne & Weinman, 1999), hemophilia (Llewellyn, Miners, Lee, Harrington, & Weinman, 2003), HIV/AIDS (Horne et al, 2004; Horne, Cooper, Fisher, & Buick, 2001a ; Walsh, Horne, Dalton, Burgess, & Gazzard, 2001), hypertension (Ross, Walker, & MacLeod, 2004), kidney disease (Butler, et al., 2004; Horne et al., 2001b), and rheumatoid arthritis (Neame & Hammond, 2005). The findings from these studies suggested a relationship between adherence and medication beliefs. Moreover, in one study, medication beliefs ($r = 0.36$; $p = < .01$) were stronger predictors of reported adherence than clinical or demographic variables (Horne & Weinman, 2002). The instrument, Beliefs About Medicines Questionnaire (Horne, Weinman, & Hankins, 1999), was developed to quantitatively measure the constructs of the theory and their relationship to adherence.

The Beliefs About Medicines framework has not been used among patients with RRMS nor with patients using injectable DMDs. Given the nonadherent rate concerning injectable DMDs among patients with RRMS, it is important to gain insight into factors that influence adherence behaviors. The Beliefs About Medicines framework may provide salient information about patients' beliefs, concerns, and overall motivations concerning the injectable DMDs.

Relevance to This Study

Patients with RRMS live daily with an unpredictable illness comprising transient symptomatology and an uncertain prognosis. Furthermore, many patients must make decisions about initiating or continuing injectable DMD that have a 30% short-term efficacy, unclear long-term benefits, and unpleasant side effects. The Beliefs About Medicines Framework may provide important insights regarding the medication beliefs

held by patients and how they influence adherence behaviors. Specifically, the constructs within this framework will help to address the following questions:

- How do patients form their personal beliefs about the necessity of the injectable DMD?
- How do necessity beliefs and perceived concerns determine adherence to the injectable DMD?
- How do intentional adherence or nonadherence (based on medication beliefs) to the injectable DMDs influence the subjective experience of patients with the management of RRMS?

The answers to these questions will help health care providers and researchers understand the experience of managing RRMS among adult women who are using injectable DMDs, have never used injectable DMDs, and have discontinued using injectable DMDs. An understanding of the experiences may lead to interventions involving support, counseling, and education that may ultimately improve patients' management of RRMS.

Chapter III

Methods

Introduction

This study used a qualitative descriptive approach to describe the experience of women as they managed RRMS. Patients with RRMS who are currently taking injectable DMDs, as well as those who have never initiated treatment and those who have stopped treatment, were interviewed about their experiences. Moreover, in concordance with the organizing framework, Beliefs About Medicines, the impact of patients' treatment beliefs on their use or nonuse of injectable DMDs were examined (See organizing framework, Figure 1). Finally, the influence of health care providers on patients' treatment beliefs and management of injectable DMDs were explored. Demographic (e.g., age, gender, marital status) and clinical data (length of time with RRMS, use of injectable DMD treatment, length of time on treatment, self-reported adherence to treatment) were collected from each participant. The Beliefs About Medicines Questionnaire (Horne, Weinman, & Hankins, 1999), was administered to describe the sample according to these beliefs and to conduct preliminary testing of the reliability of this instrument in this patient population for use in future studies.

Design Rationale

A qualitative descriptive method is desirable for this study because the subjective experience of managing RRMS among users and nonusers of injectable DMDs has not been fully explored. A qualitative descriptive approach uses naturalistic inquiry in order to "explicate the ways people in particular settings come to understand, account for, take action, and otherwise manage their day-to-day situations" (Miles & Huberman, 1994, p.

7). Naturalistic inquiry does not operate from pre-chosen study variables or a conceptual framework (Lincoln & Guba, 1985). Instead, it allows the phenomenon to emerge holistically, in context, through the perspective of the participant. The qualitative descriptive method organizes and analyzes the data, develops and consolidates themes, and summarizes and describes patterns related to the phenomenon. With minimal interpretation of the data, the subjective experience of managing RRMS is depicted exactly as it exists in patients' lifeworlds.

Setting

Recruitment of participants took place at two local health care practices. Prospective participants were identified by health care providers at an MS clinic in the UMASS Memorial Health Center/University Campus, and a neurology practice at the UMASS Memorial Health Center/Memorial Campus. The researcher brought flyers (IRB approved) to the MS clinic and neurology practice on a regular basis to recruit participants and answer questions. Patients were given a flyer containing a brief description of the study and the investigator's name and contact number. More than 720 patients with RRMS are treated at either the MS clinic or the neurology practice. Of that number, approximately 60-80% are women. The preponderance of women patients is congruent with statistics regarding gender distribution in the literature (Anderson et al, 1992).

Sample

Purposive, snowball, and theoretical sampling was used to achieve a sufficient sample for this study. Snowball sampling is a recruitment method whereby potential participants are referred by subjects already enrolled in a study (Faugier & Sargeant,

1997). Thirty-two (32) participants who met the inclusion criteria were enrolled. Maximum variation sampling was used to ensure a broad range of experiences from within the sample for comparison (Sandelowski, 1995). For example, participants ages ranged from 32 to 66; years with RRMS ranged from 8 months to 384 months (32 years); time on injectable DMD treatment ranged from 4 months to 132 months (11 years). Ongoing analysis of emerging codes and themes helped with theoretical sampling, and provided direction for further data collection (Coyne, 1997).

The sample size was determined by the number of subjects and interviews needed to achieve theoretical saturation (Morse, Barrett, Mayan, Olsen, & Spears, 2002). Theoretical saturation occurs when themes are well established and described, and nothing new is learned from participants (Lincoln & Guba, 1985). Morse (1994) suggests that 30 to 50 interviews or observations represent an adequate size for qualitative studies. Of the 32 women recruited, 25 were on treatment, 6 ended treatment prematurely, and one woman had never initiated treatment. A second interview was conducted with 3 subjects to verify data, explore new themes, and conduct member checks. Member checking involves going back to participants to clarify, correct, or validate assumptions made as the investigator analyzes the data (Lincoln & Guba, 1985).

The investigator attempted to recruit a sample that was representative of the larger population. The majority of patients with RRMS are white women (approximately 60 %) (Anderson et al., 1992). Furthermore, attempts were made to recruit patients from different races and ethnicities. The study sites had little formal statistical information regarding the racial or ethnic makeup of the population. However, anecdotal information from the health care providers indicated that a very small number of African American

and Hispanic patients were treated at the MS clinic (larger site). Researchers suggested that the predisposition to RRMS is more likely among individuals with northern European ancestry (Compston, 1997). Immigrants who are more at risk for RRMS are African Americans and Asian Americans (Joy & Johnston, 2001).

One patient who had never initiated DMD treatment and six patients who had discontinued treatment early were interviewed to gain an understanding of their perspective. An estimated 30% - 62% of patients are currently not using injectable DMD medications (Avasarala et al, 2007; Lo et al, 2005; Taylor & Leitman, 2001). The experience and perspectives of those patients may be different from those currently on the medication. Therefore, they are important individuals to interview. The health care providers at both sites had suggested that very few of their patients with RRMS who were eligible for the study were not on injectable DMD treatment.

Inclusion Criteria

Patients were eligible for this study if they met the following inclusion criteria:

1. Women age 18 and over
2. Documented diagnosis of RRMS
3. Able to understand English
4. Currently using or eligible to use DMD medications.
5. Willingness to sign an informed consent
6. Able to respond meaningfully in a 60 - minute interview
7. MMSE \geq 24

MS is a disease of young adults, affecting most patients between the ages of 20 and 50 (Jacobson et al., 1997). RRMS is rare in children; less than 5% of children

younger than 18 are diagnosed with MS (Kalb et al, 1999). Given these statistics, it was anticipated that there would be difficulty accessing an adequate sample of children. Moreover, the illness course and treatment regimens may be different for this population. Therefore, only women over 18 were included in the study. The MS clinic and neurology practice have few non-English speaking patients with RRMS; in fact, less than five non-English speaking patients are treated at the MS clinic. Given the paucity of potential subjects, it was believed that it would be difficult to accurately describe this population. Therefore, only patients who could sufficiently communicate in English were included.

Up to 60% of patients with RRMS may experience cognitive impairment, affecting attention, working memory, or information processing speed (DeLoire et al., 2005). Although considered to be mild in patients with RRMS, cognitive impairment may affect some patients' ability to respond meaningfully to the interview questions. Therefore, prior to the interview, the investigator conducted a screening Folstein Mini Mental Status Exam (MMSE) (Folstein, Folstein, & McHugh, 1975). The MMSE evaluates cognitive intactness including memory, attention, recall, orientation, calculation, and language alterations. The instrument contains 11 items, is easy to implement, and takes 10 minutes to complete.

Original implementation of the MMSE with a group of patients with various psychiatric and personality disorders, including dementia and pseudodementia ($N = 206$), and a group of non-cognitively impaired subjects ($N = 63$) yielded a test-retest reliability (Pearson coefficient) of $r = .89$ and an interrater reliability of $r = .82$ (Folstein et al., 1975). Some have questioned the use of the MMSE due to its lack of sensitivity in detecting severe cognitive deficits in MS. However, Beatty and Goodkin (1990) found

that the MMSE is an effective screen for mild focal cognitive impairment in patients with RRMS. A score of 24 (of a maximum of 30) is considered to be an appropriate cutoff for inclusion in the study (Beatty & Goodkin, 1990).

Procedures

Recruitment of Study Participants

The investigator was present at the MS clinic and neurology practice on a regular basis to recruit patients or answer questions. At other times, the health care providers (physicians, nurse practitioner) handed eligible and interested patients a flyer with the name and purpose of the study, and the investigator's name and contact information. Interested patients signed a consent form that allowed the investigator to call them. The investigator called interested patients, explained the study, and answered questions. The investigator also recruited by snowball sampling. Flyers were given or sent to eligible women, and interested women were contacted for further discussion or consent.

The investigator met with the potential participant to discuss the study, obtain consent, and conduct the screening Folstein MMSE. Interviews were conducted in an office in the UMASS Graduate School of Nursing or in a private office at the participant's work or home.

Data Collection and Management

Pilot Procedure

The entire research interview, including the qualitative interview, demographic survey, and Beliefs About Medicines Questionnaire, was piloted prior to the initiation of the study. The aims of the pilot study included: (a) to identify problems in the research design, (b) to refine the data collection process, and (c) to become familiar with the

instruments, participants, and procedures (Burns & Grove, 2004). Two individuals with RRMS known to the investigator signed a consent form to participate in the pilot. Both participants' interview forms and audiotapes were be labeled with a code and locked in the investigator's office. The participants provided feedback that helped to improve the study procedures. The pilot interviews were included in the study.

Qualitative Interview

A face-to-face, semi-structured qualitative interview was conducted, using an interview guide (See Appendix A) to elicit: (a) the subjective experience of RRMS, including the day-to-day management of injectable DMD treatment; (b) important pre-determined factors (perceived barriers, side effects, adherence); (c) treatment beliefs (treatment necessity, specific concerns); and (d) ways in which health care providers influence patients' treatment beliefs and management of the DMDs.

Specifically, the interview questions helped to address the following specific aims:

- 1) *Describe the subjective experience of patients with RRMS as they manage injectable DMDs.* Questions in the interview addressed daily life with the illness, including managing the injectable DMDs, experience of side effects, the effect of the medication on the patient's life, and adherence issues.
- 2) *Examine the treatment beliefs of patients with RRMS related to injectable DMDs.* Questions elicited the patient's views regarding the necessity (benefits) of the medication as well as their specific concerns (e.g., side effects, financial burden, etc.), and how these beliefs influenced their management of the DMDs.

3) *Examine the influence of health care providers on treatment beliefs and treatment management related to injectable DMD among patients with RRMS.* Questions addressed the patient's views on how health care providers influence their management of their injectable DMDs.

When interviewing the participants who did not initiate ($n = 1$) or had stopped injectable DMDs ($n = 6$), a modified version of the interview was used (see Appendix B).

The interview guide was revised during the study in order to fully explore new or emerging themes. Prior to the start of the interview, the investigator answered any remaining questions, reviewed the consent form, and obtained a signed informed consent. A copy of the signed informed consent was given to the patient, and the original was kept in a locked file in the investigator's office. To maintain consistency and avoid misperceptions, the investigator asked the questions from the qualitative interview first, and then conducted the demographic survey and the Beliefs About Medicines Questionnaire with the participant. The entire session lasted approximately 60 minutes. Following the interview, the participant was asked if he/she was willing to be contacted a second time to participate in one additional interview (if necessary) to clarify, explore, or verify some of the data that is being collected for the study. A list of patients agreeing to be contacted was kept in a locked file by the investigator (subjects also indicated their willingness to be re-contacted by signing a separate line on the consent form). Each participant received a \$20.00 stipend upon completion of the interview (and again if re-interviewed).

Each qualitative interview was audiotaped by the investigator. Each audiotape was identified with a research number to maintain participant confidentiality. The subject's name was not used during the taping of the interview. The audiotapes were kept in a locked file cabinet in the investigator's office to be destroyed after publication of results. The audiotapes were transcribed verbatim. Simultaneous interviewing and analysis of the transcribed tapes allowed the investigator to uncover new themes and refine the qualitative interview.

The original data forms were kept in a locked file in the investigator's office. Each form was labeled with a research number that corresponded with the number on the participant's audiotape, informed consent, and other research documents. A list of research numbers and identifiers were kept in a locked file in the investigator's locked office. The quantitative data were entered into an SPSS 12.0 file created for the study. Entered data was checked against the original data documents. Frequencies were run to examine the data for missing or erroneous entries. In addition, backup files of all entered data were created on a regular basis. Only the investigator had access to the computer containing the research files.

Quantitative instruments

The following demographic data were collected from each participant: age, gender, race, education, employment status, marital/partner status, insurance status, years since diagnosis of RRMS, type of injectable DMD treatment, length of time on treatment, and self-reported adherence (see Appendix C). The 10-item specific subscale of the Beliefs About Medicines Questionnaire (Horne et al., 1999) (See Appendix D) was also administered.

The Beliefs About Medicines Questionnaire (BMQ) (Horne et al., 1999) is a 2-section instrument, consisting of the Beliefs About Medicines Questionnaire-General (BMQ-General) (8 items) and the Beliefs About Medicines-Specific (BMQ-Specific) (10 items). The BMQ-General discerns individuals' attitudes toward medicines in general, while the BMQ-Specific assesses individuals' beliefs about medicines prescribed for specific personal use. Only the BMQ-Specific was used for the purposes of this study in order to isolate participants' views toward the injectable DMDs.

The BMQ-Specific is composed of two 5-item scales: the *Specific-Necessity* scale assesses the belief about the necessity of the prescribed medication, and the *Specific-Concerns* scale evaluates concerns about the disruptive, toxic, and dependent nature of the prescribed medication. Items are scored on a 5-point Likert scale, ranging from 1 = *strongly disagree* to 5 = *strongly agree*. The scores are summed to give a possible range of 5 to 25. Scores can be analyzed either on a continuous scale or dichotomous scale (at the midpoint), although the authors suggest that the continuous scale provides more information regarding the extent of the beliefs (Horne & Weinman, 1999). The *necessity-concerns differential* can be calculated by subtracting *concern* scores from the *necessity* scores, with a possible range of -20 to 20. The result will depict the cost-benefit evaluation made by the patient; a negative score indicates more perceived *concern* than *necessity*, and a positive score indicates a higher perceived *necessity* than *concern*. An adherence study among patients with various chronic diseases ($N = 324$) found that positive necessity-concern differential scores were associated with higher adherence rates ($r = 0.21$, $N = 324$, $p < .001$) while negative necessity-concern differential scores were related to lower adherence rates ($r = 0.33$, $N = 324$, $p < .001$) (Horne & Weinman, 1999).

The BMQ-Specific was constructed using a sample ($N = 524$) of patients with chronic illness. A preliminary Principal Components Analysis (PCA), and Exploratory and Confirmatory Factor Analyses were employed to develop and test the stability of the two factors. A replication PCA yielded identical items in the two factors.

The internal consistency (Cronbach's alpha) of the *Specific-Necessity* factor among chronic illness groups ranged from 0.55 (renal group, $n = 47$) to 0.86 (general medical in-patient group, $n = 90$). Regarding the *Specific-Concerns* factor, the internal consistency ranged from 0.63 (psychiatric group, $n = 89$) to 0.80 (diabetic group, $n = 99$). Test-retest reliabilities (Spearman correlations) among asthmatic patients ($n = 31$) were 0.77 ($p = < 0.001$) (*Specific-Necessity*) and 0.76 ($p = < 0.001$) (*Specific-Concern*). Subsequent utilization of the BMQ-Specific reported an internal consistency (Cronbach's alpha) of 0.82 (*Specific-Necessity*) and 0.71 (*Specific-Concerns*) (Horne & Weinman, 2002). This scale has not been used in patients with RRMS. Therefore, the internal consistency reliability of the scale was evaluated in the proposed sample (taking into account the small sample size).

Field Notes

At each interview session, the investigator used field notes to record observations, notes, and reflections (Creswell, 2003). The observations included participant behavior, time and setting of the interview, and other pertinent information. Reflections were related to the observations, the interview responses, or other personal insights. The field notes were organized in a notebook, labeled with an identifying number and locked with the other study documents. They were used during analysis to provide context for the data analysis (Creswell, 2003).

Data Analysis

Data analysis

The investigator used qualitative content analysis to examine the data. Qualitative content analysis uses a systematic format to develop codes, or labels, to describe data from careful reading of the interview transcripts (Morgan, 1993). A codebook was created that listed, organized, and arranged codes and data according to predetermined criteria. The purpose of coding was to cluster large pieces of data into a smaller number of focused, descriptive themes (Miles & Huberman, 1994). Codes were consolidated where possible, and ongoing attempts were made to compare and contrast patterns within and across data (Creswell, 2003). Some of the codes referred back to the organizing framework; others emerged during analysis (Sandelowski, 2000).

The codes were examined for threads of larger themes. The sampling strategy and interview guide was revised in order to explore emerging themes. A summary of the data included specific quotations or narratives that substantiated the themes. Minimal interpretation by this investigator allowed the experience to be portrayed as it was described by participants.

Quantitative data from the demographic instrument and the Beliefs about Medicines Questionnaire (BMQ) was analyzed using SPSS 12.0. The data were used to describe the sample. An attempt was made to link the quantitative data from the BMQ with the qualitative data in order to examine potential themes (Miles & Huberman, 1994).

Trustworthiness

According to Lincoln and Guba (1985), trustworthiness in qualitative inquiry relies on four components: credibility, transferability, dependability, and neutrality. The

investigator attempted to ensure credibility by spending sufficient time in the field, identifying and documenting personal *a priori* biases, correcting misconstrued perceptions through member checks, and developing a relationship of trust and confidentiality with the participants. Transferability was addressed by purposeful sampling and constructing thick, rich descriptions of the phenomenon. Dependability and confirmability involved an auditing of the research process. The investigator regularly consulted with her dissertation advisor to ensure appropriate oversight of the process; moreover, field notes and a reflexive journal were used to record reflections, decisions, and methodological issues that were encountered during the study.

Limitations

It was anticipated that there would be several limitations related to the design of this study. First, the cross-section design and small sample size prevented generalizability of the findings beyond the study sample. Furthermore, individuals who volunteered to participate in the study may not have had the same experience as those who did not participate. Finally, the limited sample size prohibited a complete psychometric analysis of the BMQ.

Protection of Human Subjects

Approval was obtained from the UMASS Committee for the Protection of Human Subjects in Research. Participants were informed about the purpose and procedures of the study. They were also told about their rights, including the assurance that: (a) they may withdraw from the study at any time without jeopardizing care (b) they may ask questions at any time during the study, and obtain a copy of the results; (c) their responses would be kept confidential and private as mandated by HIPAA, and (d) all documents pertaining to

them would be destroyed after completion of the study. Each participant was asked to sign a consent form that met IRB and HIPAA guidelines. Although unnecessary in this study, any early withdrawal from the study would have been documented and reported.

Risks

The risks involved in the interviews were minimal. The purpose, benefits, and procedures of the study were discussed with the patient. Reassurances were given regarding the confidentiality of audiotaped and written references to the participant. The interview was conducted in an unhurried, calm manner, and participants were given sufficient time to answer. Participants were reminded that they could turn off the tape recorder at any time during the interview, and the interview could be terminated at the participant's discretion. This, however, did not occur.

It is possible that a positive emotional response could occur with the opportunity to share personal perspectives with this investigator. However, particular interview questions may be distressing to the participant. Patients were told that if they become distressed during the interview, they would be asked if they wish to stop. Referral to mental health agencies or other resources for evaluation were available. However, none of the participants required referral for mental distress.

Data Management

Confidentiality with participant data was accomplished by assigning identifying number codes to each set of audiotapes, qualitative and quantitative documents, and tape transcripts. A list of codes and corresponding identifiers were kept locked in the investigator's office. Interview documents were collected, checked for completion, and stored in a locked file accessible only by the investigator. The quantitative data were

entered into an SPSS 12.0 database on a laptop computer with an access password known only to this investigator.

Conclusion

The purpose of this qualitative descriptive study was to examine the subjective experience of women as they managed RRMS and DMD treatment. In addition, beliefs about the DMDs and the influence of health care providers in patients' treatment beliefs and management of injectable DMDs were explained. Patients with RRMS who were currently undergoing injectable DMD treatment, as well as those who never initiated or who had stopped treatment, participated in the study. The organizing framework, Beliefs About Medicines, guided the study. Common themes related to the phenomena emerged. Qualitative content analysis was used to analyze the interview data, and descriptive statistics were used to analyze the demographic and BMQ-specific results.

Chapter IV

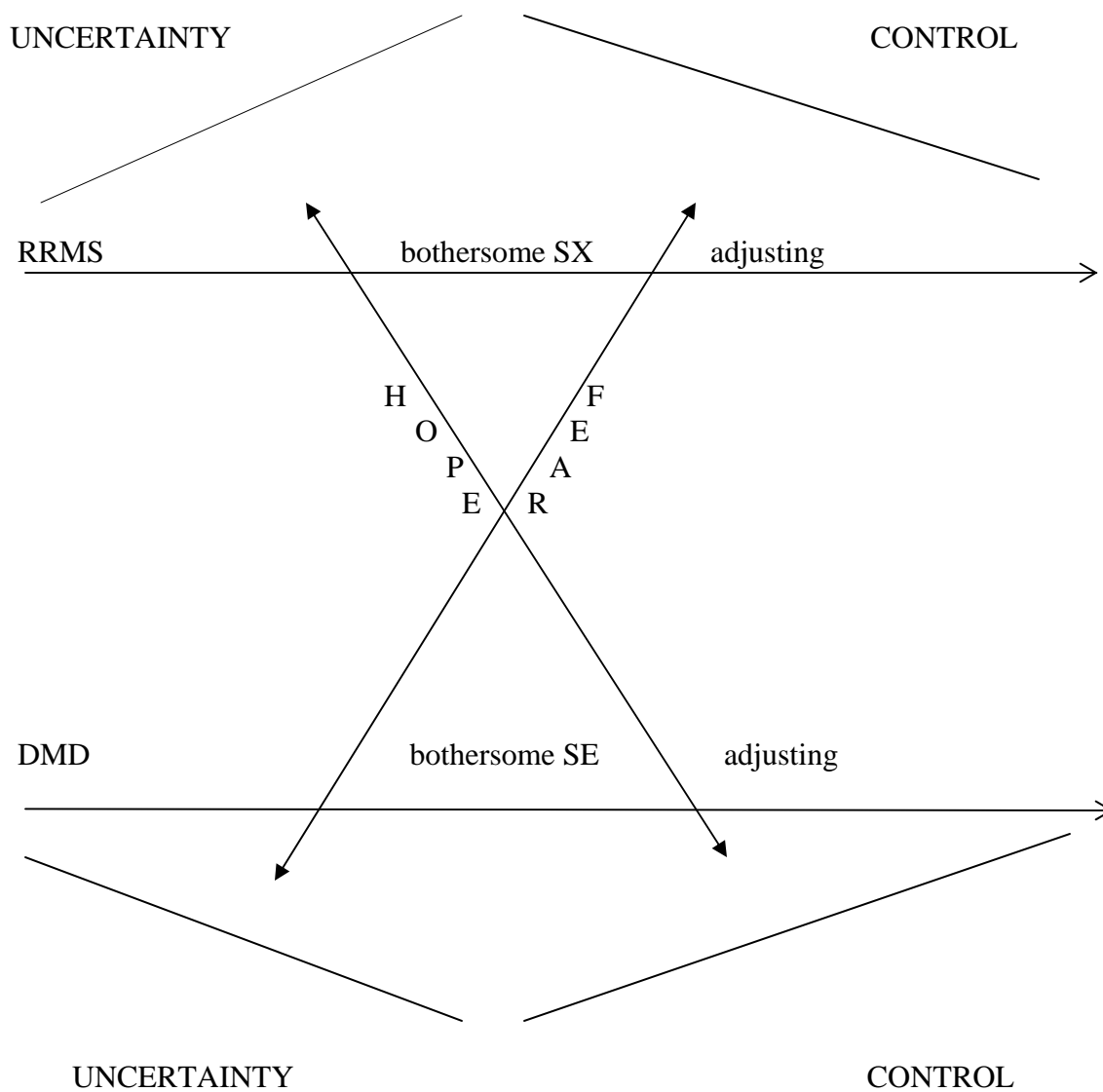
Results

Qualitative descriptive methodology was used to study the subjective experience of the day-to-day management of RRMS among adult women who were currently using injectable DMDs, had stopped using injectable DMDs, or had never used injectable DMDs. The results revealed two overarching themes, *Uncertainty* and *Control*, and three subthemes, *Adjusting (limitations, changes, strategies, and attitude)*, *Bothersome Symptoms/Side Effects* and *Motivation (fear and hope)*. Sample characteristics and a description of the overarching themes and subthemes, with illustrative participant quotes, follow. The results are organized by each study aim. The themes and subthemes are depicted in a schematic as a parallel process. (Figure 2) Results for the first two aims will be presented in an integrated manner.

Participants

A total of 32 women were recruited for a one-time, face-to-face interview which lasted approximately 60 minutes. Interviews took place in a private room at UMASS Memorial Health Care Center ($n = 19$), at participants' work ($n = 4$), or in their home ($n = 9$). Prior to the interview, each participant completed the Folstein Mini Mental Status Exam (MMSE). All of the women scored greater than 24 on the MMSE. Each qualitative interview was followed by a demographic survey and the Beliefs About Medicines Questionnaire (BMQ). Recruitment was ongoing until the researcher determined that information redundancy was reached and no new information was revealed. The data collection occurred from February, 2006, to June, 2006. Frequencies were run and revealed no missing data from either the demographic surveys or BMQ instrument.

Figure 2. A Parallel Experience of Managing RRMS and Injectable DMDs



Key:
RRMS: Relapsing-remitting multiple sclerosis
DMD: Disease Modifying Drug
SX: Symptoms
SE: Side effects

Ninety-four per cent of the women were white, which is consistent with the overall prevalence of individuals with RRMS by race (Anderson et al., 1992). The mean age was 47. Most of the women were married or living with a partner (91%), reported having a post-secondary education (75%), and were working at least part time (72%). Four of the women (12.5%) were nurses. The average length of time with RRMS was 99 months (8.2 years). The average length of time using injectable DMDs was 37 months (3.1 years). Demographic characteristics of the sample are contained in Table 8.

Use of Injectable DMDs

Of the total number of participants, 25 women were using injectable DMDs, 6 discontinued injectable DMDs, and 1 never started injectable DMDs. The most commonly used injectable DMD was IFNB-1a IM (Avonex) followed by glatiramer acetate (Copaxone), IFNB-1b (Betaseron), and IFNB-1a SC (Rebif). Six women (19%) switched to their present therapy from a prior DMD; three of those women switched more than once. The most common change was from glatiramer acetate (Copaxone), a non-interferon DMD, to IFNB-1A IM (Avonex), an interferon DMD. The most common reason for switching was worsening disease ($n = 5$). Two women who discontinued treatment reported switching DMDs (once). A record of DMD usage is located in Table 9.

Overarching Theme and Subthemes

Two overarching themes and three subthemes emerged from women's responses regarding their experiences. The overarching themes, *uncertainty* and *control*, were present in all interviews. Issues of *control* were integrated throughout the data. Women described *adjusting* to RRMS, including *limitations* and *changes*. They also described a

‘parallel experience’ in managing their RRMS and their injectable DMDs, which encompassed *bothersome symptoms/side effects*, and *strategies*. Women discussed developing a *positive attitude* to adjust to the bothersome symptoms and uncertainty. *Fear* and *hope* were described as motivators for continuing treatment; they intersect with women’s parallel management of their RRMS and injectable DMDs.

Aim 1: Describe the subjective experience of women’s day-to-day management of RRMS among those who are currently using injectable DMD therapy, have never used DMD therapy, or have stopped using injectable DMD therapy.

RRMS: Bothersome Symptoms

Bothersome is defined as “causing annoyance and inconvenience”

(www.encyclopedia.com/dictionary).

Most of the participants ($n = 28$) reported having bothersome symptoms or functional impairments. The most common symptoms or impairments included fatigue, difficulty walking, cognitive issues (memory, thought processes, word recall), and numbness. Commonly reported symptoms are listed in Table 10.

Fatigue was reported as the predominant and most distressing symptom. Two women termed their fatigue ‘depressing.’ One woman claimed that MS was called the ‘tired disease.’ Common characteristics of fatigue included: occurring later in the day; exacerbated by the lack of sleep, heat and excessive activity; and requiring naps or rest periods. One woman’s fatigue was increased before her menses. One woman described the intensity and unpredictability of her fatigue: “I get half way through the market and feel like I couldn’t take another step. An’ I have left my stuff and gone home. Or not gone to do the next errand. I just — it can be so sudden.”

The women described their walking problems in terms of balance issues, leg pain, weakness, and limping. One woman described her leg pain, “I will get leg spasms occasionally but they don’t last . . . for 12 hours or less, and they really don’t affect my walking ability . . . and they seem to come when I am very tired.” Other women stated that their foot dragged, causing them to limp, especially when they were tired or walked long distances. Four women discussed monitoring their legs, when walking, to avoid tripping or falling. “If I spend a lot of time walking and stuff. . . I have to really pay attention to where my leg is, so I make sure it doesn’t, like, give out on me or. . . that I don’t trip or fall.” One woman described having to ‘mentally tell her legs to move.’ Another woman needed to arrange her living space to avoid injury from falls. “. . . even just getting out of bed, I don’t know if my legs are going to hold me up. . . if the kids leave a toy there or my husband, the socks on the floor, I still have to make adjustments.”

Cognitive issues included problems with memory, word recall, and thought processing. The most common complaint was memory loss. Women also reported forgetting words or misplacing items. Two women mentioned a more severe memory problem.

Um, the only piece that never changed in that way is I can read a book and I cannot tell you what the book is about when I get to the end. I can go to the movies and watch a movie and I cannot tell you what the movie is about when I get out. I don’t remember it.

Others suffer from word recall. One woman stated, “It’s just — I can start a sentence and I can’t find a word that I’m looking for. And it just makes me shy away from talking to people at times.”

Women reported facial, limb, and genital numbness. The most common numbness occurred in the hands. One woman described the sensation:

It's almost like, how I explain to my children, I said, put a glove on your hand.

That is what my hand is like every day. Pretend you have to try and wash dishes with that glove on. You have to zipper your coat or button your jacket or make dinner with that glove on. That is what it feels like for me. . . . on a bad day I said now put a mitten on you and try zippering your jacket. That is the best way that I can explain the numbness there.

The numbness was transient for some but constant for others. Women reported stress ($n = 2$) and warm water ($n = 2$) as precipitators of the numbness. One woman described the effect of numbness in her hands on her fine motor skills. "Sometimes I can't put my earrings in or the clasp of my chain. . . . then I just get mad, and yell, 'I can't do this.'" A woman reported that genital numbness negatively affected her sexual relationship and ended her marriage with her husband.

Uncertainty

All of the women described a sense of uncertainty related to RRMS. Women discussed uncertainty about the future ($n = 11$), including becoming a burden, having to be in a wheelchair, having to stop working, or what would happen to their children. Other areas of uncertainty included relapses ($n = 6$), functional status ($n = 5$), MS-related symptoms ($n = 3$), course of illness ($n = 3$) and worsening disease ($n = 3$). One woman described each uncertain day as a "grab bag." "My family knows, I say to them, it's like a 'grab bag' every morning. I wake up and think, okay, what's it going to be like today? Will I be able to walk? Will my vision be bad?" A woman with few symptoms described

the effect of constant uncertainty: “It’s like always in the back of my mind. Um, the wondering, like, what’s going to happen to me...am I going to continue feeling the way I do. . . . or is the bottom going to fall out. . . . and *when?*” Another woman referred to the unpredictability of relapses, “It sucks, in plain English. . . . you don’t know when it’s going to hit you again. . . . you have to live day to day.”

One woman described how she hid her feelings of uncertainty: “Outwardly, I pretend nothing is wrong with me and I’m just fine. . . . inwardly, it’s so uncertain that I don’t know what tomorrow is going to bring.” Another woman described how uncertainty prevented her from making future plans. “. . . . You want to make plans for retirement and we want to do this and go here. . . . I would like to be excited about these things. . . . but are we ever going to be able to do those things?”

Adjusting: Limitations, Changes, Strategies, and Attitude

Adjusting (adjust) is defined as “to adapt to a new environment or condition” (<http://encarta.msn.com/dictionary>). Women described ways that they had adjusted to their RRMS through terms like “compensating,” “modifications,” “accommodating,” and “making changes.” “But really, my life, the whole picture has been like one big compensation. I just fit my life into the MS.” Some women ($n = 10$) described their RRMS positively, using terms such as “normal,” “stable,” “mild,” “healthy,” and “not very difficult.” “I work the same. I am still taking care of my kids and going to their functions. I do everything that I normally do. I just get a little more tired at night.” One woman said, “It’s normal living. . . . only every day when you get your butt out of bed. . . . you say ‘Thank you, God’ and you just go on and do your day.” Other women ($n = 15$) used more negative terms, such as “discouraging,” “frustrating,” “difficult,” “a

challenge,” and “depressing.” Two women described their bodies as being “out of control.” Yet, even with negative terms, some women described how they adjusted. “It’s discouraging sometimes. . . . I live with it. . . . I try to make people laugh. . . . if I’m making somebody else laugh, then I feel like I’m laughing, too.” A woman stated, “It’s a little depressing. . . . you can deal with it, you know?” Another woman said, “You learn to live with it. . . . it’s what life dealt you.”

Women’s adjustment to their RRMS did not seem to be influenced by the number of years with RRMS or current treatment status (on treatment, off treatment, never started treatment). For example, one woman with RRMS for 4 years (and not using DMDs), stated, “I do everything everybody else does but. . . . I get really tired. . . . I just don’t have the energy to do the things I want to do. . . . I keep going.” Another woman with RRMS for 10 years (and using DMDs) said, “It’s discouraging sometimes. I try to cover it up as best as I can. It’s just — it’s not what I had expected at this point in my life the loss of physical use on my right side.” A third woman, who has lived with RRMS for 22 years and never started DMDs, reported issues with balance, memory, numbness, and bladder control. Yet she stated, “I would have to say, to me, it’s a perfectly normal lifestyle, like everyone else’s lifestyle.” Women described limitations and changes in their lives due to bothersome symptoms and uncertainty.

Limitations

Women described limitations on their life due to their RRMS. Persistent or bothersome symptoms, including fatigue or impaired walking, limited activities such as extensive walking ($n = 11$), participating in social events ($n = 8$), and housework ($n = 4$). One woman described having to limit her walking distance and speed. “You’re limited as

to how much you walk because you get too tired.” Some women reported that bothersome symptoms forced them to limit their housework. One woman described how she had to do her housework in segments: “I get up and I start my breakfast and take it easy. . . . I do something and I’ll sit down and relax a little while. . . . laundry. . . . that’s about it.” Another woman described how fatigue caused her to limit her errands. “It’s like, I can’t go to Walmart and the grocery store on the same day. . . . ’cause if I do, I’m exhausted.”

Some women described how they had to acknowledge that certain activities were no longer possible. “I used to take my dog for walks. . . . I can’t now because my foot drags.” Yet, other women purposely continued with their routine. “I deliberately walk my dog every day and I deliberately go up and down stairs. . . . and go to the market. . . . but often, by the end of the day, I’m tired and my left leg will drag a little.”

Three women described how their RRMS affected their social life. One woman stated, “Well, the social life — you go out. . . . you cannot really do nothing but sit there and look at people.” Another woman said, “. . . your friends will spend the day doing something and then go for dinner. . . . then go dancing. . . . I have to go home. . . . I feel like I’m holding my husband back. . . . he’s saddled with me.” Some women also discussed the limiting impact of RRMS on their family activities. Women described difficulty in attempting to play with their children or grandchildren, attend their children’s activities, or enjoy summer vacations or outdoor activities in the sun.

Despite limitations, some women described important functions they were able to manage. One woman stated, “I had to sell my business. . . . it was very hard to work the way I was and have MS. . . . I’ve still been able to maintain a house, a home, raise a

family and enjoy everything I've ever enjoyed." Another woman described how she overcame her limitations. "It (RRMS) doesn't limit me. . . . either I've gotten used to things like my slight residual numbness in my feet or learned to work around it."

Changes

Women discussed the changes that occurred in their lives with RRMS, including changed self-identity, relationships, priorities, and plans. Women described how their RRMS caused changes in their self-concept. One woman talked extensively about the significant impact her RRMS had on her self-identity. "I went through a year and a half to two years of hell just in — in getting a grip on. . . . who and what I was going to be as a person with MS — because my identity changed." Another woman stated, ". . . . I'm not perfect. . . . there's something wrong with me." Two women with fatigue and walking impairments jokingly referred to themselves as 'old lady.' Many women ($n = 8$) compared their condition to others with MS; some felt grateful that their illness was not as extensive, while others worried that they might someday experience similar disease progression. "But I see people at church that have it...and I see what they're going through. . . . on disability, not working. . . . is that going to happen to me?"

Women discussed the change in relationships with family and friends due to the RRMS. One woman who had difficulty initially accepting her diagnosis spoke of her need to leave friendships during her transition. "I've come to a place in my life where I've accepted what's going on with me. . . . this is my reality, and I have got to get my life around it, and if you can't, I have to leave you behind." She described discovering new friends who were willing to listen and help her to redefine herself with her illness. Another woman described the variability of responses by others to her RRMS: "There are

times when. . . my close friends or family. . . they're either over-solicitous, 'Oh are you sure you can do this? Are you tired?' or they just think I can do the same things. . . I always did."

A woman described her family's transition as she adjusted to her RRMS: ". . . they were treating me with kid gloves and, um, I don't have that personality. . . it was hard for them to know how to deal with me. . . they are much more accepting and ready to talk about things and deal with things." One woman worried about the added responsibility her RRMS put on her husband. "You know, my husband is — he's also retired. It's put more responsibility on him. Physically and mentally. He hates when I don't feel well. You know, and he worries about me, which I feel real bad about."

The diagnosis of RRMS caused many women to evaluate their current situation and future plans. Women discussed changing priorities to minimize the effects of RRMS and maintain their quality of life. Women modified educational goals, vacations, and retirement plans. One woman described how she scaled back her goals to accommodate her RRMS. "I used to be a very high goal setter. . . because I got sick, I wasn't able to do as well as I anticipated. So I kind of minimize what I think my maximal potential could be." Another woman discussed her decision to actively pursue her goals after her diagnosis. "So what can I do today because it's something I should do or always wanted to do, and ten years from now I may not be able to?" She described her plans to further her education.

Two women spoke of changing vacation plans because of heat intolerance, while two other women described scheduling long-awaited vacations earlier while they were functional. "My husband and I will take more vacations than we did before, that type of

thing. Because there are things I want to see and I'm still able to do that." Four women discussed engaging in healthier lifestyles, including exercise, diet, and smoking cessation. Four other women described plans to make permanent adjustments to their houses in anticipation of the future.

Strategies

Women described strategies to control the physical impact related to RRMS, including modifying their environment or lifestyle and managing symptoms. "I get things done in completely different ways." A list of symptoms and strategies are in Table 11.

Some women reported being sensitive to triggers of their RRMS symptoms, and adjusted their environment or lifestyle to avoid them. Four women identified stress as a trigger to the onset of symptoms, which include fatigue, limping, neuropathy, and vision changes. "Stress seems to be a trigger, at least for me. I have certain symptoms like that numbness. . . . It's almost like an indicator. I have to calm down and relax whatever the stress or heat or severe cold sometimes."

Many women ($n = 10$) accommodated their fatigue by avoiding the heat, taking naps, adjusting work, asking for help with chores, and slowing down. One woman had air conditioning installed to minimize the effects of the heat. Some women ($n = 4$) verbalized frustration that they had to nap or rest during the day. "I take naps. . . . that's something I didn't used to do. . . . sometimes it bothers me that I just can't get through my whole day without a nap. . . . that part is hard to adjust to." Others ($n = 4$) spoke of 'pushing through' their fatigue as a way of maintaining a normal life.

Six women reported that they had altered their work life due to the RRMS. Some women retired early ($n = 2$), while others stopped working ($n = 2$) or reduced their

schedule ($n = 2$). One woman perceived the decision to leave her stressful job as a positive change for herself and her family. “So we decided to see if we could try to make do without me working. . . . without the MS diagnosis, I don’t know if we would have made that decision. In one way, it has actually helped.” Another woman described how having to stop working negatively affected her social life: “I mean, I’m not saying work is great. . . . but it was just — it was a way out, you know, and then you can talk with other people. . . .”

One woman laughingly described how she resolved her reluctance to let others help in the house. “. . . it was hard for me to give up control over. . . . how the house is managed...I still try to do that by having the person who is ‘best suited’ for the things I need them to do.” Two women discussed how learning to slow down had a positive effect on their life. “I was always on the go. . . . but I never enjoyed what I was doing. . . . now I notice the flopping of the dog’s ears, or I notice my daughter is laughing a little bit deeper or longer. . . .”

Some women described addressing their walking difficulties by monitoring their legs, walking with others, and utilizing supports. “Because I have weakness in my left leg, I always have to be paying attention to what that leg is doing so that I don’t trip.” One woman described how she no longer took walks alone: “I used to go out walking a lot, you know. . . . alone. . . . I’ve had a couple of falls, and I just — I prefer to have someone around me.” One woman described how pushing her grandchildren in their stroller allowed her enough balance to continue taking walks.

Two women reported using handicapped license plates to conserve energy and accommodate walking abilities. Three women with cognitive difficulties spoke of writing

things down to remind themselves of important tasks or appointments. Two women described having to read and reread material to refresh their memory.

Positive attitude

Women's attitudes toward their RRMS were important components of adjustment to the RRMS. One woman reported that taking a proactive approach in managing her illness helped her to have a positive attitude. "Kind of altering your lifestyle and making things a little bit easier for you. Understand your limits, I think, has a lot to do with how well you do." Another woman stated, "I guess you make changes. You do modifications. Other than that, I just live life like I don't have MS. You know, I look on the bright side of things. I keep positive in my attitude." Another woman stated, "I don't let MS rule my life. . . . I refuse to as long as I can." One woman asserted that she maintained control of the RRMS, "You have to be the boss of your body. . . . I have MS but MS isn't going to control me. . . . I'm the boss."

Attitudes were dependent on women's illness status. One woman stated her lack of symptoms over the years made it easy for her to cope. ". . . the fact that I haven't had symptoms and it's now been going on six years since my official diagnosis, you start feeling like, okay, I can live with this." Three other women described their RRMS as a "mild case," and asserted that their attitude might be different if their status changed.

Two women focused on the things they could still do; for example, raise a family, work, or walk the dog. Some ($n = 4$) had the attitude there was nothing they couldn't do, and were doing everything they wanted to at that time. "I've learned to live with what I have and again, I am just going to do as much as I can." Three women discussed using humor to cope with their RRMS. One woman stated, "The day the doctor told me I had

MS, I said to him, ‘Good, now I can park in those places with the little round chairs.’”

Other women ($n = 4$) reported that their faith helped them adjust to the diagnosis. “With my faith, I know that and I’ve accepted what — the disease I have and I know that through my faith, I have to continue this course. This is what’s been offered to me.”

Injectable DMDs: Bothersome Side Effects

As part of their management of their RRMS, most women ($n = 25$) were currently using DMDs. More than half of the women using injectable DMDs (56%, $n = 14$) reported experiencing flu-like symptoms as the most common systemic side effect. Women described a constellation of symptoms, including headache, fever, chills, chest discomfort, insomnia, and muscle pain. Flu-like side effects were most often reported by women using interferon-beta 1a IM (Avonex) ($n = 11$), interferon-beta 1b (Betaseron) ($n = 2$), and interferon-beta 1a SQ (Rebif) ($n = 1$). One woman described how she felt after the injection: “the next day. . . . I’ll say to my husband, I don’t even feel human today.” Two women stated their flu like symptoms were constant; one of the women expressed distress at causing her symptoms, “It’s painful. My chest gets really. . . . I curl up. . . . in a fetal position. Every muscle tightens. . . . and it’s hard, knowing that I’m doing that to myself.” She confessed that she would skip injections or squirt out medication to avoid the severe side effects. Other side effects included elevated liver function tests ($n = 2$), low back pain ($n = 2$), and production of antibodies ($n = 1$).

Three women reported their side effects had diminished over time. However, nine women reported that the symptoms were variable and unpredictable. In fact, one woman questioned whether her occasional insomnia and ‘hot flash’ were due to the injectable DMD or menopausal symptoms. The side effects could appear several hours after the

injection and last up to 48 hours. One woman compared the unpredictability of the DMD treatment effects to the unpredictability of her RRMS: “I used to try Advil at night. . . . but it’s almost like MS itself. . . . sometimes, the medicine, you respond differently on days. . . .” The flu-like side effects seemed to be influenced by the injection location, time of day, adequate hydration, and premedication with analgesics. Injection into the arms seemed to intensify the side effects and injecting into the buttocks mitigated the side effects. Most of the women (88%, $n = 22$) reported injecting their DMD at nighttime to allow them to sleep through side effects.

Women described missing work or social events due to the occurrence of severe side effects. Some women stated family and friends knew to refrain from calling or visiting after the injection. “People know not to call for a couple of days. When I make plans, it has to be towards the end of the week. So it’s changed the way I do things.”

Adjusting: Attitudes and Strategies

Adjusting to the injectable DMDs included the perception by women of their ability of women to control or cope with its impact on their lives. Eleven women used positive terms in describing their management of their DMD therapy, including “easy,” “a piece of cake,” “no big deal,” “just a routine,” “so automatic,” and “part of my life.” Three women stated how they “fit it into their life.” An equal number of women ($n = 11$) used negative terms to describe their experience: “I don’t love it,” “extreme inconvenience,” “horrible,” “gives you the heebie jeebies,” “I hate it,” and “worst part of the disease.”

Women used terms or phrases that depicted how they perceived their DMD, including “insurance policy,” “empowering,” “part of the big plan,” and “something to

believe in.” Other participants described the injectable DMDs as “not so bad” and “bearable.” A woman felt that her attitude toward the DMD diminished its negative effect: “It’s not an inconvenience in my life. It’s my lifesaver. It’s a different mindset.”

Some women described how the injectable DMDs had become a routine part of their life. “. . . it’s so automatic. . . . now it’s just part of my life. . . . I’ll do this every other night and hopefully it will keep things at bay. . . .” Another woman said, “It’s just like brushing my teeth. . . . it’s like what you do. . . . it’s part of my daily routine.”

Three women described how their DMD increased their quality of life. “It’s made my quality of life better. . . . it has allowed me to do the things I’ve wanted to do.” Another woman claimed, “It’s going to give me a good life.” Women stated they used the injectable DMDs because they wanted to keep walking and did not want to “get worse” ($n = 8$), or “end up in a wheelchair” ($n = 6$). Three women discussed feeling responsible to use the injectable DMDs; one, a nurse, stated, “I’d feel. . . . if something did happen and I got more lesions, I’d feel like. . . . I’m not trying to make myself better.” Another nurse expressed, “I’m in the health care profession. . . . I believe in. . . . trying to treat a problem. . . . can’t leave everything in God’s hands.”

Women described the importance of control while using the injectable DMDs. Two women indicated that using the DMDs made them feel in control; one said, “. . . . the biggest thing I feel is in control. . . . when you can do something so small to give yourself a sense of being in control. . . . it is something you can do that’s positive.” Another asserted, “So if giving yourself a shot every day is going to help you control the MS, which you have absolutely no control over anyway, then you put up with a little grief.” In referring to the negative aspects of the DMDs, one woman stated, “So, again,

it's an inconvenience, but you can control that.” Conversely, a woman who discontinued DMD therapy reported feelings of lack of control. “The medicine made me feel like. . . . I didn't have control of me. . . . I just didn't feel like myself.” Women described strategies that helped them to adjust to their DMDs.

Strategies

Women described their strategies concerning management of their injectable DMDs in great detail. Women chose days of the week and times of the day that were convenient for them. Most of the women received their injection at night and at home. Almost half of the women ($n = 12$) premedicated with either acetaminophen or ibuprophen to mitigate side effects; other women stated they felt they no longer needed to premedicate due to reduced side effects. Nine women reported rotating sites arms, legs, buttocks and hips. One woman advised, “Find a healthcare professional that can really stab you in the butt. . . . it has eliminated pretty much all of the side effects and the ones that still linger are very manageable.”

Other strategies included the use of ice, a calendar or schedule, an injection grid (to keep track of rotating sites), and a quiet place. One woman described how she ‘personalized’ her regimen: “I had a cardboard box for the longest time. . . . I finally said this is for me. . . . I have to do something nice. . . . I bought myself a nice tray.” She reported that the special tray was a helpful reminder to take her shot. Common injection issues or side effects and useful strategies are located in Table 12.

Sixty-four percent of women ($n = 16$) reported never skipping their injectable DMDs, while 36% ($n = 9$) skipped one or more doses. Reasons given for skipping medication included vacations ($n = 4$), emotional distress ($n = 3$), and bothersome side

effects or injection issues ($n = 3$). One woman described feeling ‘in control’ when she decided to skip an injection: “. . . it’s just sometimes you get fed up with everything and it’s one thing you have control over. . . .” Another woman described getting angry at her DMD, “I’ve looked at those injectables and I just picked it up. . . . I’m not taking you tonight. . . . I was angry at it. . . . I guess it was just my way of dealing with it that night.” One woman described skipping many daily injections due to painful skin reactions before finally switching to another injectable DMD. She professed to ‘feeling guilty’ and that she ‘was failing them’ (health care providers) by skipping her doses.

Six women reported occasionally missing an injection due to forgetting, procrastination, or illness. One woman reported feeling guilty for missing a shot. “It’s like Monday night. . . . my husband’s already asleep, he can give it to me tomorrow night. . . . in the back of my mind, I need to take my medication. . . . if I tell my mother, she’s all down my throat. . . . I feel even more guilty!” One woman, who was a nurse, emphatically denied skipping injections. “Absolutely not. The nurse in me would never allow that to happen!”

Aim 2: Examine treatment beliefs, including treatment necessity and perceived concerns, related to injectable immunomodulator therapy among women with RRMS who are using or not using injectable DMD therapy.

Aim 2 is presented using both quantitative and qualitative data. The Belief About Medicines Questionnaire (BMQ) was utilized in this study to determine women’s beliefs about their injectable DMD. The BMQ consisted of 10 statements using a 5-point Likert scale that ranges from strongly disagree (1) to strongly agree (5). The *necessity-concerns differential* was calculated by subtracting *concern* scores from the *necessity* scores, with a

possible range of -20 to 20. The results reflected the cost-benefit evaluation made by the patient; a negative score indicates more perceived *concern* than *necessity*, and a positive score indicates a higher perceived *necessity* than *concern*. Despite the limited nature of our sample ($N = 32$), the internal consistency reliability (Cronbach's alpha) was 0.89. Therefore, the BMQ has good reliability in this sample. The results from the BMQ can be found in Table 13, and will also be integrated with the qualitative findings. The necessity-concern differential will be included in the discussion under Treatment Concerns.

According to the Belief About Medicines framework (Horne and Weinman, 2002), patients' treatment beliefs are influenced by information or experiences related to the prescribed medicine, and perceptions of personal identity and control. Patients participate in a continual process of weighing *perceived needs* for the medication (e.g, to improve or maintain health) against *concerns* regarding the medication's effect on day-to-day living (Horne & Weinman, 2002). Feelings of uncertainty and control were threaded throughout women's responses about their beliefs regarding the injectable DMDs. Several women described a process of 'weighing the pros and cons' in deciding to start or continue the injectable DMD treatment. Most women identified *fear* and *hope* as motivators for continuing treatment.

Treatment Necessity

Treatment necessity is the belief that a particular medication is essential for treatment. Perceived need is individual and may be influenced by several factors, including beliefs about medicines in general, prior experience with the medication, illness beliefs, filtered information, and social or cultural expectations. Five statements in the

BMQ addressing women's beliefs about treatment necessity are integrated with the qualitative data.

Three statements on the BMQ addressed women's perceptions of treatment necessity related to maintaining their present and future health and preventing disease progression. Based on the responses, women believed that their present and future health depended on the injectable DMDs. In response to the statement, "My *present* health depends on the injectable DMDs," 44% per cent ($n = 14$) agreed, 34% ($n = 11$) disagreed, and 22% ($n = 7$) were unsure. When addressing the statement, "My *future* health depends on the injectable DMDs," 59% ($n = 19$) agreed, 22% ($n = 7$) disagreed, and 19% ($n = 6$) were uncertain. Moreover, women responded that the injectable DMD treatment kept them from getting worse.

Regarding the statement, "The injectable DMDs keeps me from getting worse," 81% ($n = 26$) agreed, 13% ($n = 4$) disagreed, and 6% ($n = 2$) were uncertain. Almost half of the women using (or having used) DMDs (46%; $n = 13$) reported no change in their RRMS symptoms since starting the DMDs, while 36% ($n = 10$) described their status as "better," and 18% ($n = 5$) indicated that their condition was "worse." Fifty-nine per cent ($n = 19$) of women reported having no relapses over the last year; 25% ($n = 8$) had one relapse, 13% ($n = 2$) had 2 relapses, and 3% ($n = 1$) had five relapses. Three of the women who had discontinued DMDs reported experiencing worsening disease despite treatment.

Fifty per cent ($n = 16$) of women reported that they received information about the injectable DMDs from their health care providers; other sources of information were websites (38%; $n = 12$), nurses (9%; $n = 3$), and books or magazines (3%; $n = 1$). Most

women understood that injectable DMDs ‘prevented or reduced the frequency of relapses’ ($n = 15$), followed by ‘delayed progression’ ($n = 10$), and ‘prevents new lesions’ ($n = 7$). Women articulated that while they were not a ‘cure,’ they believed the DMDs would delay progression and reduce the frequency of relapses, using terms like “maintain,” “holding pattern,” “keeping MS at bay,” “slowing it to a crawl,” “stabilizer,” and “status quo.” One woman stated, “. . . and I know that remittent MS can turn into progressive. . . . my outlook is if I’m on the medication, I’ll never turn into progressive.” Another woman said, “I learned that it’s best to stay on your medicine. . . . it will help you stay ahead of it, of getting more attacks. . . . lesions. . . . I don’t want to get worse.” However, a woman who discontinued using injectable DMDs described how her physician refuted assumptions that the injectable DMDs delayed progression: “She said (the effect) is almost anti-inflammatory. . . . it turns it down a little bit but it’s not slowing the progression of the disease. . . .”

Uncertainty

Uncertainty was a common theme in women’s discussion of their beliefs about treatment efficacy. Sixty-four per cent of women using DMDs ($n = 16$) and 50% of women who had discontinued DMDs ($n = 3$) said they weren’t sure if the medication worked. One woman stated, “Do I think it works? I have no idea.” Another woman said, “What is it really, really doing?” Furthermore, many women expressed uncertainty whether their current stable health was due to the medication’s effects. Three women attributed their current condition to having a ‘mild disease.’ However, one woman stated that the reason for her stable disease was immaterial:

So what changed? Was it the medication? Was it attitude? Was it lifestyle? Was it something I'm drinking or eating or breathing? I don't know. But if it's the medication, good. If it's got nothing to do with the medication, oh well. So I have a few bumps.

Another woman said, "Is it working? I'm walking and talking, so whether it's doing something or not. . . . I'll take that chance."

Half of the women indicated that they were uncertain about what would happen if they were not on the injectable DMDs. When answering the statement on the BMQ, "Without the injectable DMD, I would be very ill," 50% ($n = 16$) of women were uncertain, 31% ($n = 10$) disagreed, and 19% ($n = 6$) agreed. One woman professed, "I think I wouldn't feel as good as I do. . . . I THINK. . . . but I don't know." Another woman who experienced bothersome side effects stated, "On days that I don't want to do Avonex any more, I think nothing would happen. . . . I would be fine and this would be as bad as I'd get. . . . so I just don't know. It's a crap shoot." Others stated, "I'm assuming it's helping me," and, "Well, I haven't had any flare-ups so I would say it's better, if the medication is working." One woman felt that if she worsened, it was 'her own fault,' not the medication.

Finally, in response to the statement, "My life would be impossible without the injectable DMD", 66% ($n = 21$) of women disagreed, 19% ($n = 6$) were uncertain, and 16% ($n = 5$) agreed. Two women who had discontinued the DMDs reported their life actually became more manageable after stopping. One woman stated, "I felt like I was clearer in the thinking. My legs were a little more stiff but I figured I could deal with that versus how else I was feeling. I couldn't eat. . . . couldn't sleep. . . . I just didn't like it".

Perceived Concerns

In the Belief About Medicines framework (Horne & Weiner, 2002), *perceived concerns* are anticipations of unpleasant adverse effects or disruption by a particular medication, including long term effects. Concerns may develop from concrete experiences with the medication, misinformation, or miscommunication between the health care provider and patient. Five statements in the BMQ addressed treatment concerns; the results will be integrated with the qualitative data. Concerns regarding the injectable DMDs caused some women to either switch or discontinue their treatment.

Twenty-four percent ($n = 5$) of women using injectable DMDs switched medications; of those, two women switched twice. The most common reason for switching was worsening disease ($n = 4$), followed by injection site reactions ($n = 1$), and increased liver enzymes ($n = 1$). All of the women who switched reported improvement over the prior DMD.

Nineteen percent ($n = 6$) of the women reported discontinuing their injectable DMD therapy. Two of the women who discontinued had switched medications; one reported switching twice before stopping. Common concerns among the six women who discontinued involved both concrete experiences with the DMDs and beliefs about the DMD therapy. Concrete experiences included bothersome side effects ($n = 4$), disruption of plans ($n = 4$), and injection issues ($n = 4$), fear of needles ($n = 2$), painful injections ($n = 1$), injection site skin reactions ($n = 1$), having others inject ($n = 1$). Concerns related to beliefs about the injectable DMDs were perceived mild disease ($n = 2$), perceived worsening disease ($n = 2$), and uncertainty regarding the effects of the DMDs ($n = 1$).

Necessity-Concerns Differential

The necessity-concerns differentials were calculated for each participant, and can be found in Table 14. Most of the differential scores ($n = 24$) were positive, indicating beliefs in treatment necessity. However, eight differential scores were negative, reflecting women's concerns about treatment. The woman who never started injectable DMDs had a negative differential score, as did five of the six women who discontinued DMDs. The sixth woman had switched treatment twice due to ineffective DMDs, and then discontinued the third injectable DMD due to severe skin site reactions. She stated that she did not want to stop treatment. "I tried it for two more weeks. . . . it's not that I don't want to . . . I can't. . . . it hurts. . . . it's not worth it." Therefore, according to her negative differential score, the woman believed treatment was necessary, but her severe skin site reactions caused discontinuation. The woman was scheduled to start an intravenous treatment.

Two women who continued using injectable DMDs had negative differential scores. One woman expressed doubt about her diagnosis, felt well, and described a negative concrete experience with the injectable DMD, including painful injections and bothersome side effects. The woman described skipping injections, reducing the dose, and considering stopping. Therefore, bothersome side effects while feeling well caused more concerns than belief in treatment necessity for the woman.

The other woman described how she had discontinued treatment on her own once before in order to become pregnant, and only resumed due to worsening symptoms. She considered the injection "poison" and described "feeling well" off treatment until a bout of optic neuritis. The woman stated that she had originally thought she could manage her

RRMS without treatment, and even with resuming, was already considering stopping to conceive another baby. Therefore, while having more concerns than beliefs in treatment necessity, the woman continued with her injectable DMD due to disease worsening while off treatment.

Injection Issues

Injection issues were problematic side effects of the injectable DMDs. Twenty-nine percent of women ($n = 9$) reported having a general dislike of needles. “And even after 500 times doing this, every week, once a week, that needle in my leg, I still have a hard time with it.” Two women using glatiramer acetate (Copaxone) complained about having to undergo daily injections. Anticipation of injections caused emotional distress for some women, including “anxiety,” “nervousness,” “agitation,” “anguish,” and “dread.” One woman described the anticipation, ‘just the thought of it,’ as ‘hanging around in my head’. Specific problems with injections included injection pain ($n = 13$), skin reactions ($n = 17$), and having others inject ($n = 6$).

The injection pain was described as ‘stinging,’ ‘smarting,’ and ‘sore.’ One woman explained that the pain was unpredictable. “Some nights it hurts, ‘n some nights it doesn’t. You never really know until you hit the injector if it’s going to hurt.” Some women indicated that their pain was from the medication rather than the needle. Some women ($n = 2$) described an itchy sensation at the site. Both the interferon and non-interferon injectable medications caused skin reactions, although painful lumps were more common with the non-interferon DMD (glatiramer acetate). The skin reactions ranged from mild bruises to hard, painful lumps or sores. One woman discontinued her therapy and another woman switched injectable therapy due to severe skin reactions.

“But I would always have an injection site reaction, a big, red, hot lump probably 2-3 inches across that would stay for a long, long time. . . . it was just — it was hard to do it every day.” Some women reported having to locate new injection sites due to the residual lumps. Most women reported rotating injection sites.

One woman discussed the impact of her injection skin reactions on her relationship with her husband. “He’s afraid to touch me because sometimes I feel tingly...or, you know, to touch me where I gave myself a shot because it might be a little tender that day. . . . he waits for me to tell him what to do. . . .” She stressed how important it was to her relationship to have him feel like he could physically touch her, despite the discomfort it caused.

Some women described how the injection process took up a lot of their time. Women described sitting for minutes or hours, delaying the injection. “I was doing it at 7:00 every night. . . . I’d be lucky if I shot myself in the leg by 8:30. . . . I just HATE doing it.” One woman described her emotional distress during the process. “One day I sat here, and I was telling the dog to hit my hands so I wouldn’t have to do it. I mean, I was in tears.” The woman ultimately asked others to administer the injection. Many women, however, reported that the process eventually took less time. Several women discussed the mental preparation that was involved before the injection. A woman whose husband was the injector stated, “I try to remind myself. . . . the week before, the needle didn’t hurt so bad...it’s not going to hit a bone. . . . then I close my eyes and hold my breath.”

Taking the injectable DMD on trips or vacation was a concern for some ($n = 4$), and was one of the reasons that one woman discontinued her treatment. “So we went to Florida with my daughter. . . . and I didn’t want to take it (IFNB-1b) because it has to be

refrigerated and everything. So I just didn't take it and I haven't taken it since." Women discussed having to make special arrangements for transporting the IIM during travel and vacations. Several women reported packing ice and injection supplies with little difficulty; however, other women reported omitting or delaying injections rather than carry the DMDs. In fact, the most common reason given for skipping or missing a dose was going on vacation.

Other injection issues involved having others help with injections. While nine women self-injected, six women chose to have others give all their injections, and ten women self-injected with occasional help. 'Other-injectors' included family members, friends, or health care providers. Some women had others inject due to their needle phobia or to access hard-to-reach locations (arms, hips, buttocks). Sometimes having another person inject posed a dilemma for women. One woman said her main injector, her daughter, was moving, and she wasn't sure how she'd manage. Two other women felt it was more inconvenient to have others inject because of the planning and travel involved. However, one woman who had discontinued her injectable DMDs believed she would resume if another person would administer her injections.

General views about taking medicines influenced some women's concerns about the injectable DMDs. Five women described being reluctant to use the injectable DMDs, or any type of medicine at all. One woman who had discontinued the DMD stated, "I'm not really into the medication thing. . . . I don't like what. . . . that kind of drugs do to you. . . . I need to stay focused. . . . not be drugged out." Another woman using DMDs described how having to use an injectable DMDs changed her self-concept: ". . . . That I'm not infallible. . . . not invincible." Specific concerns regarding the injectable DMDs

included having to plan, insurance issues, lack of active disease, disease worsening, and uncertainty related to medication effects.

When responding to a statement on the BMQ regarding whether the injectable DMD disrupted their life, 78% of women ($n = 25$) disagreed and 22% ($n = 7$) agreed. However, many women reported having to arrange their activities around their injections. Depending on the DMD therapy, injections were administered every day, every other day, or once a week. The DMDs were refrigerated, and required several hours to warm to room temperature. Sometimes women forgot to remove the DMDs from refrigeration, and either tried to warm it quickly, or, sometimes, they just skipped the injection. “By the time I remember I’m going to take it, you have to wait for it to warm up a little bit and then I don’t want to. So I won’t take it.” One woman described how the injectable DMD regimen dictated her plans. “I was just at my mother’s house helping her with something. . . . I wouldn’t feel comfortable saying, ‘Oh, I think I’ll stay over’, because I don’t have my medicine with me. . . . so it makes decisions for you.”

Only two women described having difficulties with insurance coverage. However, both women were able to find alternate means to pay for the medication. One woman described the frustration of having to quit her job to be eligible for public assistance (MassHealth). Another woman expressed uncertainty about affording the medication due to her husband’s retirement. “Because my husband retired...we don’t have no more insurance. If I don’t get. . . . the help, I’m not going to do it. I’m not going to pay no \$1,400 a month.” She was receiving her medication at no cost through one of the medication companies, but was not going to continue her DMD without financial assistance.

Six women indicated that the DMDs had a greater impact on their life than their RRMS. Many of these women had few symptoms of RRMS but suffered great discomfort from the injectable DMDs. Two women ultimately discontinued DMDs because they ‘felt well’ with the RRMS, while at the same time they were experiencing bothersome side effects from the DMDs. “It was hard to reconcile in my head. . . . why stress myself out like that every other night when I’m really feeling well?” Conversely, a woman who continued stated, “Sometimes I feel like I’m taking the medication and I’m not sick because I feel so good. . . . now I have come to terms with I’m not sick BECAUSE I’m taking the medication. . . .”

Thirty-two per cent ($n = 8$) of the women who were currently using injectable DMDs reported the onset of new symptoms or new lesions (on MRI). One woman who was currently using DMDs described her uncertainty related to the worsening disease; “. . . maybe without the Avonex, I would have ten lesions. . . . it’s a crap shoot.” Another woman reported that her new symptoms were mild compared to past symptoms. “My last attack was in December. . . . wasn’t as bad as it could be. . . . this time it was just one leg, so that was pretty good.”

However, 33% ($n = 2$) of the women who discontinued DMDs attributed their worsening disease to the injectable DMDs. One woman described having increased relapses; another woman reported the increased impairment that severely impacted her employment. “I either had three or four (relapses) and I had to go on IV steroids and I was pretty much ready to quit work. . . . had to use a cane. . . . I felt like I just couldn’t go on.” Both women claimed that their symptoms improved after discontinuing their injectable DMDs. One woman described her improvement, “It’s like being locked in

your room for a year and all of a sudden you get out. . . . because I spent a lot of time in my bedroom. . . . I was just out cold.”

Two of the statements on the BMQ addressed concerns regarding immediate and long term effects of the injectable DMDs. In addressing the statement, “Having to take the injectable DMDs worries me,” 53% ($n = 17$) of women disagreed, while 47% ($n = 15$) agreed. Furthermore, when responding to the statement, “I sometimes worry about the long-term effect of the injectable DMDs,” 59% ($n = 19$) of women agreed, 34% ($n = 11$) disagreed, and 7% ($n = 2$) were uncertain. Finally, when answering the statement, “The injectable DMD is a mystery to me,” 66% ($n = 21$) women disagreed, 22% ($n = 7$) agreed, and 12% ($n = 4$) were uncertain.

Several women expressed concerns related to the uncertain effects of the injectable DMDs. One nurse who discontinued her DMD after only one injection described seeing the effect of the DMD on another woman “. . . . I saw one patient (on injectable DMD). . . . and really, I didn’t see any changes. . . . as a matter of fact, she was getting worse at some points. . . . what is it really, really doing?” Another woman who was using an injectable DMD worried that her DMD might be masking worsening disease, “. . . . what if I have fifteen more lesions. . . . and I don’t even know it because my medication is hiding it. . . . I’d like to have more MRIs. . . .”

Addressing the last of the five statements related to treatment concerns, “I sometimes worry about becoming dependent on the injectable DMDs,” 88% of women ($n = 28$) disagreed, 3% ($n = 1$) agreed, and 9% ($n = 3$) were uncertain. Despite the concerns regarding the injectable DMDs, most women expressed a commitment to continue with treatment. However, four women reported that they had considered stopping treatment.

One woman described being doubtful about her diagnosis, while also suffering severe side effects from the DMD. She reasoned that stopping the DMD would improve her quality of life. : “I’d rather get. . . . ten good years now than a slow twenty years. . . . I only have two. . . . three good days a week, where if I stop, I’ll get my seven. . . .”

Another woman described her struggle between wanting to stop and having to continue: “I keep doing it and. . . . I don’t know if it’s working . . . the hell with it, I’m just not going to do this anymore. . . . but then, when I don’t do it, I say this is stupid. . . . you know you have to do this. . . .” One woman wondered how long she would continue: “Sometimes I don’t know how many years I’m going to feel like doing this.” Other women ($n = 4$) discussed taking a break from the treatment. But, as one woman said, “I’ve definitely asked about taking a break and then going back. . . . but how long do I need a break...take a week, a month...I’m not going to tell myself I’m taking the summer off. . . . life doesn’t take time off.”

Motivation: Fear and Hope

Motivation means “to give a reason or incentive to do something”(www.encyclopedia.com).

Fear and *hope* were identified by many women as motivators of continuing with injectable DMD therapy. Seven women mentioned that they would not stop their injectable DMDs because they feared worsening disease or disability. “When you start any treatment that you start for the MS, you have to stick with it. . . . because then your fear is that if you don’t, you are going to be in a wheelchair.” Another woman stated, “I always thought, OK, I have relapsing-remitting MS. . . . I never thought it could get

worse, but yes it can. . . . that scares me. . . . that really gives me the motivation to keep the injections going.”

One woman described being afraid of recurrence of her prior relapse, “I’m in fear of what might happen. . . . my left side. . . . just the numbing, burning. . . . my right side was weak. . . . I could barely write. . . . couldn’t lift my leg. . . . I just didn’t like the feeling at all.” One woman reported having resumed treatment because she had an onset of optic neuritis. “When I stopped taking it, I thought, I can live this way...my quality of living wouldn’t be degraded that terribly. . . . now having the optic neuritis, that’s a little scarier for certain. . . .”

Fifty-six percent ($n = 14$) women referred to the injectable DMDs as their only hope to control their RRMS. One woman stated, “Knowing that right now this is the only hope I have in keeping my disease in remission. . . . I continue regardless of what the side effects are.” She spoke of two friends who had died of MS; she felt that, unlike them, she was given ‘a gift.’ She believed that, without the therapy, her friends had no hope. Other ‘hopes’ shared by women were that the DMDs would work, that they could continue with the medication, and that an oral medication would soon be available.

One woman, expressing uncertainty, implied both hope and fear. “Why do I take it? Because it might work. . . . you don’t know. . . . but I do it because. . . . I don’t know what it would be like if I didn’t do it.” Another woman, when asked about her long term plans, said, “. . . . just want to take this journey or this ride for what it is right now until something better comes along that offers more hope.”

Four women described a process of ‘weighing the pros and cons’ in deciding to start and continue with their DMDs. One woman described her decision-making process

when starting, “There was definitely a little bit of weighing pros and cons. . . . I mean there are no guarantees. . . . I chose Rebif.” One woman explained, “Well, I know the flu symptoms. . . . and all that. . . . you’ve got to weigh the pros and cons and to me, anything you take nowadays has side effects and long term effects, so. . . .” Another woman stated, “I look at it as if it can benefit me more than it can hurt me. . . . that’s why I’m on it.” Conversely, one woman who had discontinued after only one injection many years ago stated, “What real benefit is it going to be for me? I’ve learned to live with my body the way it is now. . . . with my disease the way it is. . . . why start a new treatment now?” ‘Pros and cons’ described by women are listed in Table 15.

Two women talked about taking risks with the injectable DMDs. One woman said, “It’s a risk. . . . I know life is full of risks, but right now, I’m stable. . . . if that’s the price I’m going to pay in my mind, then that’s it.” Another woman stated, “. . . if it was going to maintain me, I do pretty well in between anyway. . . . why take the risk?” Eight women professed not wanting to ‘take a chance’ of stopping their DMDs. “I have stayed exactly the same. . . . I don’t really know if I would have stayed that way had I not started the medicine. . . . I don’t want to take the chance to stop it and see what the end result will be.”

During a re-interview with participants (member checking), one woman described her motivation to continue using her DMD as ‘blind faith.’ She felt that she had to have faith and hope that her DMD would continue to maintain her in remission and prevent progression. However, she said, “It’s a blind faith. . . . you may know what side effects you get, but you don’t know if the medication is working. And you have to have blind faith that, somehow, you are going to be better.” Another woman described it as ‘the less

uncertain road.’ She believed that using the DMD was at least more certain than continuing with RRMS without any treatment.

Aim 3: Examine the influence of health care providers on treatment beliefs and management of injectable DMD therapy among adult women with RRMS.

Women’s attitudes toward their health care providers were mostly positive. They described general characteristics of their health care providers. They also described the quality of their interactions with health care providers concerning the initiation, continuance, or discontinuation of the injectable DMDs. Finally, they discussed the influence of their health care providers on their management of injectable DMD.

Women described positive characteristics of their health care providers, including ‘a good listener,’ ‘available,’ ‘easy to talk to,’ ‘doesn’t rush you,’ ‘caring,’ and ‘compassionate.’ Other women, however, described attributes of their health care providers as ‘kind of rushy,’ ‘not talkative,’ and ‘distant.’

Women described the availability of their health care providers during and between visits. “They’re busy. . . . but not so busy that if I needed to talk. . . . they’re a phone call away.” Another woman said “Even though they’re seeing hundreds of patients, when they are with you, they make you feel like you’re the only person that they have.” One woman said: “They spend the time with you. . . . it’s not like you go in there and they go over this list, and you’re there for 15 minutes. . . . and out the door.” However, one woman felt that her visit with her health care provider was ‘rushy.’ She stated that she tended to avoid asking her health care provider.

Women described how their health care providers listened, explained, and encouraged discussion. Four women reported that their health care providers actively

listened. One woman stated, “He absolutely listens to you. . . . listens to what you have to say...listens to what your feelings are.” Another woman said of her health care providers, “Their compassion and their understanding and their ability to listen...is remarkable for as busy a practice that they have.” The woman believed her health care providers’ caring and concern were the reasons she continued working with them. However, one woman, who did not believe her health care provider understood her concerns, felt that ‘being heard’ was essential. “I think. . . . that the neurologist should LISTEN to the patients. . . . and not look at their watch a lot. . . . so that you feel that you’re being heard. . . .”

Women discussed how their health care provider shared information with them. One woman said, “They’re easy to talk to. . . . and they explain everything. . . . answer all my questions.” Another woman stated: “If they want to try something different, they’ll explain to you. . . . it’s HOW they explain what they want to do for you. . . . it’s the overall caring they give you.” She went on, “And they made me having the MS more relaxed because they do care. . . . and you know that they are there if you need them. . . .” A woman stated, “They act like it really matters.. . . . your input. . . .”

However, one woman felt as though her concerns are not always taken seriously. “The things that I think are. . . . new things for me or more difficult. . . . or are related to MS, he will sort of *pooh pooh*. . . . ‘that’s not an MS thing’. . . . and I really don’t understand.” She reported that she did not share many of her concerns with him. Another woman stated she would like her health care provider to ‘see’ beyond the neurological disease. “He could be a little bit more. . . . just talking and asking more questions about things outside of just the straightforward neurological things.” A woman did not feel her health care provider could understand her experience. “He doesn’t feel that I’m getting

any worse...but I feel inside like, 'you don't know what I'm feeling' . . . and is not understanding how a little thing like your hand being numb can be just devastating some days. . . .”

Three women described having confidence and trust in their health care providers. “. . . And I know my doctor's on top of things. . . I know he'd be here to help me and to give me any input I needed. . . that's a matter of having confidence in my doctor.” Another woman said, “I fully trust him and if he says that I need it, then I guess that I need it (medication).” One woman stated, “He's the head of Neurology; he must be a good person. . . so I feel in safe hands.” A woman described her confidence in her doctor as equal to her confidence in her injectable DMD. “It's a combination of having as much confidence as I can in the medication but more than that, the healthcare providers are. . . equally important. . . I just have complete confidence in them.” One woman described how her health care providers gave her a sense of control. “when you get to a point where don't feel like you have control of your own body, your own life. . . and there is somebody there that gives you a possible hold or remedy, they're your best friend.”

Another woman who discontinued her DMD due to severe injection site reactions described her confusion after discussing her worsening disease with her health care provider “. . . he went over the medicines. . . it is supposed to be helping me. . . the radiologist saw significant changes in the MRI. . . when I talk to him [health care provider]. . . he says there isn't any. . . it's weird.” One woman said of her health care provider, “...MS is like an unknown. . . nobody knows what's going to happen. . . I

know that he doesn't either. . . . he's not God. . . . he doesn't know what's going to happen next on my MS in particular."

Women described how they and their health care providers made decisions regarding their general care. Some women said they followed their health care provider's recommendations. One woman stated, "I'm an easy person. . . . I go with what the doctor tells me." Another woman said, "I think I'm a little bit afraid of him [health care provider]. . . . he kind of has that scary attitude sometimes. . . . 'you do as I say'. . . . so you do it." However, two women stated it was important to be partners in their healthcare. One woman described a 'good working relationship' with her health care provider. "He allows me to dictate. . . . he allows me to be a partner in my own healthcare." Another woman stated, "I like to be part of the decision-making. . . . I don't want to be in the situation where I'm told what to do."

Women described the initial discussion with their health care provider regarding injectable DMD treatment. Eight women reported that their health care provider gave them materials to review and to select one of the four injectable DMD. "So he really left it up to you. . . . he didn't recommend one or the other. . . . here's the pros and cons. . . . they leave it up to the patient." Conversely, seven women reported that their health care provider suggested a particular DMD. Six women described doing research on the injectable DMD, and preferred to make the decision: "I think it's definitely a benefit that they leave that up to you. . . . it's your choice. . . . it's in your hands, but they give you enough information to make that decision."

Other women wanted help with selecting the 'right' DMD. "I would rather say, 'here, you take this. . . . because this is a good one'. . . . I've chosen the Avonex, but

maybe the Rebif is the real good one.” One woman described the uncertainty of choosing the right medication. “It was a hard decision for us. . . . what was right. . . . A, B, or C. . . . just throw it up in the air. . . . it was like trying to make an educated guess without really knowing.” Another woman described the importance of making the decision for herself: “It was my decision to start on the medication. . . . my decision which one I decided to go with. . . .”

Women described the discussion about the management of their injectable DMDs during their health visits. Six women reported that they felt they discussed their injectable DMDs enough, especially if they had questions or concerns. However, health visits did not always include discussion about the injectable DMD. Seven women claimed the topic usually did not come up. Many women asserted that their health care provider would discuss any problems if they arose. “He’ll ask about any problems. If things are going well, we don’t usually talk about it.” One woman stated, “I think they just assume that I’m taking it. . . . and it doesn’t like really come up, like, ‘do you take, do you not take It’. . . . you know ‘are you taking it faithfully?’” Another woman described how her health care provider discussed alternative plans in case the treatment didn’t work. “He said if it didn’t work. . . . I could try out any one of the other medications. . . . so far, it seems to be working. . . . so we are sticking with this one.”

Women described how their health care providers advised them regarding the use of injectable DMDs. One woman who sought a second opinion about her diagnosis related her physician’s view regarding when to start using injectable DMDs; “. . . and she wasn’t convinced that I have MS. . . . she was saying it’s one-third of the year. . . . that you don’t feel well. . . . she had a difference of opinion when you should start this

medicine.” The woman discontinued her DMD in consultation with her health care provider. She went on to assert that, if she experienced symptoms, she would consider beginning treatment.

A woman with RRMS for 22 years, who never started injectable DMDs, professed a similar experience with her physician: “He said, ‘I will let you know, I don’t believe it’s (your RRMS) ready. . . . you don’t have to take it right now. . . .’” Another woman with mild symptoms who has been using DMDs for 3 years reported that her health care provider thought she might be able to discontinue someday. “. . . the doctor said that. . . . if I continue like this, maybe I won’t have to use the medication long-term...if I don’t have any more attacks after a few years. . . .”

Women who discontinued injectable DMD therapy described their discussion with their health care providers. Of the six women who discontinued DMD therapy, four women discontinued without first consulting their health care providers, one woman informed her doctor, and one woman stopped in consultation with her health care provider. The discussion between the health care providers and women who stopped without consultation occurred weeks or months after the women had been off of the medication. One woman described her health care provider’s reaction: “He wanted me to continue. . . . he was very upset with me at the next appointment because I had just not given him the chance to make that decision with me.” She believed their conflict affected their rapport: “I called the office. . . . I had some significant pain issues. . . . it was the next day when I got called back. . . . (He) and I went toe to toe. . . . so I don’t feel as comfortable going to him.” She planned to schedule visits with an associate health care provider.

Another woman described a more positive experience when her health care providers learned she had discontinued treatment. “They asked why I’m not on it and I told them. . . . they really didn’t push me that much, not like they were before.” She was surprised that their reaction was so mild. She explored alternative treatments with them.

A woman who discontinued her injectable DMD described feeling understood by her health care provider. “She’s compassionate enough to know that I don’t feel comfortable being on that med. . . . she would want me to. . . . but she understands.” All but one woman who discontinued injectable DMDs have continued regular visits with their health care provider. One woman has not seen her health care provider in three years. “I haven’t seen him for about three years. Last time I saw him he said, ‘if you have a problem, call me’. . . . haven’t had one so I haven’t called.” Another woman who discontinued treatment after receiving a second opinion described a positive relationship with her health care provider: “I don’t think (he) was happy about it. . . . but he still wants to see me. . . . as a matter of fact, he wants to see me more. . . . just so I don’t fall out of the loop.”

Some women reported that, although they received information and support from their health care provider, continuing to use the injectable DMDs was still their decision to make. One woman stated, “I don’t feel he’s (health care provider) got all the answers for what I should be doing, with my MS, and taking Avonex or not.” Another woman said, “I don’t think they have any impact at all (on my management of the DMDs). . . . when it comes down to it, the decision is mine. . . . I’m the one who decides every week that I’m going to do it.” Another woman said, “They can say, oh, make sure you take your medicine but I have to make the decision to do it.” One woman described how

health care providers should counsel their patients about initiating DMDs. “If they were to just explain the benefits of it, to let them know it is *their* decision.”

Summary

In summary, two overarching themes, *uncertainty* and *control*, and three related subthemes, *Bothersome Symptoms/Bothersome Side Effects*, *Adjusting* (limitations, changes, strategies, and attitude) and *Motivation* (fear and hope) emerged from women’s descriptions of their experiences managing RRMS. Analysis of the data revealed that, whether or not they were using injectable DMDs, most women experienced limitations or changes related to their RRMS, including physical, emotional, or relationship transitions. Limitations varied depending on bothersome symptoms and uncertainty. Women developed strategies to control their bothersome symptoms and maintain an optimum level of function. Women also used positive attitudes to cope with the uncertainty, limitations, and changes.

Women’s experiences included a parallel of managing their RRMS and injectable DMDs. While managing their bothersome symptoms, women who were using injectable DMDs encountered similar difficulties managing unpredictable and bothersome side effects. Some women skipped, switched or discontinued their DMDs due to their difficulties, while other women controlled their DMDs through developing strategies and having positive attitudes.

Women also continued or discontinued their injectable DMDs based on treatment beliefs, including treatment necessity and treatment concerns. Most women who believed that treatment was necessary had stable or improved symptoms or minimal side effects. Women who discontinued their DMDs had no symptoms (‘felt well’), had intense side

effects, or had worsening disease. However, some women continued with their DMDs despite worsening disease or bothersome side effects. Both women who continued and discontinued DMD treatment had information and support from their health care providers. However, both groups also expressed uncertainty regarding treatment efficacy. Women maintained control by making decisions to continue or discontinue their injectable DMDs.

Women weighed the ‘pros and cons’ of the injectable DMDs to decide about initiating and continuing treatment. Some women who continued the DMDs expressed more benefits, while women who discontinued the DMDs expressed more concerns. Women who were uncertain expressed hope in their treatment and fear that stopping treatment would worsen their RRMS. They continued using their DMDs with ‘blind faith’, uncertain about the treatment effects. Yet, women viewed continuing the DMDs as a ‘less uncertain road’ than trying to manage their RRMS without treatment. This study highlighted the experiences of women with RRMS who were using or not using injectable DMDs, including day-to-day management, treatment beliefs, and health care provider influence. Awareness of these unique issues is important when planning strategies to educate, counsel, and support women with RRMS.

Chapter V

Discussion

The purpose of this study was to gain an understanding of women's experiences of managing RRMS, including using injectable DMDs. This topic was important because few studies have examined the parallel experience of managing RRMS and injectable DMDs. Findings from the descriptive summaries revealed that women experienced unique changes and limitations related to their RRMS; however, women adjusted through maintaining a positive attitude and developing strategies to manage their bothersome symptoms. Similarly, women adjusted to their DMDs through a positive attitude and developing strategies to manage bothersome side effects. Treatment adherence was influenced by women's parallel RRMS/DMDs experience, women's treatment beliefs, and health care provider influence.

Uncertainty and control were important components of the parallel experience, and influenced women's beliefs. Health care providers offered information and support; yet, women were uncertain about treatment efficacy and long-term effects. Despite the uncertainty, most women continued treatment, while others discontinued their injectable DMDs. Hope and fear were perceived as motivators of continued treatment. This chapter will address current findings and existing literature related to uncertainty, treatment beliefs, and health care provider influence.

Uncertainty

Mishel (1988) defined uncertainty in illness as "the inability to determine the meaning of illness-related events [that] occur in situations where the decision-maker is unable to assign definite values to objects and events, and/or is unable to accurately

predict outcomes because sufficient cues are lacking” (p. 256). Mishel’s Uncertainty in Illness model (1988) was derived from Lazarus and Folkman’s (1984) work on stress, appraisal and coping. Mishel’s models of Uncertainty in Illness (1988, 1990, 1997, 1999) are commonly used in nursing research and practice.

According to the Uncertainty in Illness model (1988, 1990) uncertainty is an inherent aspect of chronic illnesses such as RRMS. Factors that may cause or exacerbate uncertainty in chronic illnesses include ambiguity regarding the illness, complexity of treatment and care, inconsistent information from authority figures, and unpredictability of the illness course or outcome (Mishel, 1988). Adaptation is largely dependent on personal attributes, social supports, and appraisal of the uncertainty (as a danger or an opportunity).

Mishel (1988) suggested that individuals who identify uncertainty as a danger may attempt to reduce uncertainty through information-seeking, vigilance, and garnering social support. On the other hand, perceiving uncertainty as an opportunity may cause some individuals to control, rather than reduce, uncertainty through maintaining a sense of hope. Uncertainty may allow some individuals to maintain a sense of hope in illness conditions that might otherwise evoke helplessness or hopelessness. Mishel (1988) suggested that, under these circumstances, maintaining uncertainty may yield more positive outcomes, such as adherence to treatment or medications. Controlling uncertainty involves focusing on positive cues (information, comparison to others, improvement in health status) and prioritizing one’s life.

Mishel’s framework is effective in explaining women’s experiences in this study. Women described a pervasive uncertainty in living with and adjusting to RRMS and

injectable DMDs. Uncertainty encompassed unpredictable bothersome symptoms and treatment side effects, relapses, daily functional status, disease worsening, and future outlook. Women's adjustment to their RRMS varied, with most women indicating that 'you just live with it' and 'you learn to deal with it'. Some women described a constant mindfulness of or vigilance over their condition, while others indicated that they never thought about their illness until their DMD injection day. All of the women described ways in which they had incorporated the RRMS into their lives. Women controlled their RRMS by developing strategies to manage their bothersome symptoms and avoid relapses. Some women made plans for advanced education, early retirement, travel, and vacations.

These findings are consistent with others related to RRMS found in the literature (Courts, Buchanan, & Werstlein, 2004; Jopson & Moss-Morris, 2003; Kroencke, Denney, & Lynch, 2001; Miller, 1997; Vaughan et al., 2003). Although published a decade ago, Miller's (1997) study revealed that individuals' adjustment to RRMS mirrored the adjustment experienced by the women in this study. Participants described experiencing a sense of loss of control due to uncertain symptoms and relapses, and regaining control through maintaining a positive attitude and developing strategies. Miller (1997) suggested that individuals who had adjusted well had learned to control their symptoms and maintained a sense of optimism. It was unclear whether these individuals were using injectable DMDs.

More recently, Thorne and colleagues (2004) found that patients' (with MS, non-specified) fear due to illness uncertainty was initially managed through seeking information from external sources, including health care providers, Internet resources,

and MS support agencies. However, patients subsequently described adjusting to their illness by re-ordering priorities and developing effective management strategies. They perceived that ongoing support with information from health care providers was essential as they managed their changing functional abilities, difficult or unpredictable symptoms, and optimization of their health. Other findings related to uncertainty, perceived control, and adjustments were reported in the literature (Courts et al., 2004; Jopson & Moss-Morris, 2003; Kroencke et al., 2001, Russell, Kilburn, Conn, Libbus, & Ashbaugh, 2003; Vaughan et al., 2003).

It is conceivable that perceiving uncertainty as an opportunity motivated some women to initiate and continue use of injectable DMDs. Some women described having a sense of control in undergoing treatment with injectable DMDs. Verheggen and colleagues (1998) found that individuals ($N = 52$) facing uncertainty were more apt to agree to participate in a clinical trial. However, uncertainty can also negatively influence patients' adjustment and subsequent behavior. Wineman and colleagues (2003) found that patients with greater uncertainty and greater disability were likely to be less hopeful and experience negative adjustment to their RRMS.

In summary, Mishel's Illness Uncertainty model explained women's experiences in this study. Women managed uncertainty through developing strategies, re-ordering priorities, and maintaining a positive attitude. Uncertainty caused women to seek information from health care providers and other sources. Finally, women perceived uncertainty as an opportunity and sustained hope for the future and hope in the injectable DMDs.

Beliefs About the DMDs

The Belief About Medicines framework (Horne, 1997), suggested that 1) patients' behaviors regarding medicines were influenced by their beliefs, including treatment necessity and treatment concerns; 2) a predominance of one belief over the other would predict behavior; and 3) patients engage in constant monitoring of their treatment beliefs, and their behavior changes with changing beliefs. Treatment beliefs are based on general beliefs held about medicines, concrete experience with the medications, and information from others, including health care providers. The BMQ elicits treatment beliefs, and its *necessity-concerns differential* determines the predominance of one set of beliefs over the other.

Treatment Necessity

The Beliefs about Medicines framework explained the behavior for most of the women in this study. Qualitative data was congruent with the quantitative results of the BMQ. The findings suggest that most women were ambivalent about treatment effectiveness. The majority of women agreed that the injectable DMDs improved their present and long term health. Perceptions of treatment necessity were regarding stable health, decreased relapses or symptoms, feeling in control, and having a sense of hope. Women based their positive beliefs on symptom experience as well as information from health care providers, Internet sites, and reading materials, such as magazines.

However, fifty percent of women were uncertain whether they would be very ill without treatment. Almost half of the women in the study reported no change in their symptoms while on treatment. Moreover, forty-one percent of women reported having one or more relapses over the last year. Therefore, women were unsure whether the

injectable DMDs were instrumental in stabilizing their RRMS. While not a cure, DMD treatment is modestly effective (30%) in reducing the frequency of relapses. However, residual symptoms and even new symptoms can persist despite adherence (Calabresi, 2002). Patients may need reassurance that even without obvious signs, the injectable DMDs are working to minimize neuroinflammatory damage.

Women (66%) disagreed that their lives would be impossible without the injectable DMDs. These women may have experienced stable health without improvement, worsening health, or unpleasant effects from the injectable DMDs. Several women reported that their quality of life improved after they discontinued treatment. Assessing patients' experiences and beliefs regarding their injectable DMDs is important in order to develop informational and support strategies.

Treatment Concerns

Six women discontinued injectable DMDs in this study. Treatment discontinuation ranged from 1 week to 2 years, consistent with the literature (Ruggieri et al., 2003). Type of injectable DMD was not a factor in discontinuing treatment, as has been suggested in the literature (NARCOMS News, 1999; Ruggieri et al., 2003). Two women discontinued IFNB beta-1a IM, two women discontinued IFNB beta-1b, and two women discontinued glatiramer acetate. The adverse effects were not specific to an injectable DMD. For example, bothersome side effects were caused by IFNB beta-1a IM and IFNB beta-1b; worsening disease was caused by Interferon beta-1a and glatiramer acetate.

Five of the six women who discontinued using the injectable DMDs had a negative necessity-concerns differential score, indicating more concerns than treatment

necessity. The sixth woman, who had discontinued her DMD due to severe skin injection site reactions, had a positive necessity-concerns differential score. She felt that treatment was still necessary despite overwhelming injection issues. The woman was prescribed an intravenous infusion treatment, consistent with treatment guidelines (National Multiple Sclerosis Society, 2005). Discontinuing treatment in this study is consistent with adherence behavior described by Meichenbaum and Turk (1987). Deliberate non-adherence may result from a decision by individuals to maintain control of and improve their quality of life.

An interesting finding was that two women who were using the injectable DMDs had negative scores, indicating stronger beliefs regarding treatment concerns over treatment necessity. One of the women had expressed doubt in her diagnosis, had described painful injections and severe side effects, had skipped or reduced the dose, and was considering stopping treatment. The other woman had stopped for a year due to a pregnancy, and decided to stay off treatment because she had few symptoms. However, due to a sudden bout of optic neuritis, she contacted her health care provider and resumed the DMD. Although she is currently using her DMD, she still reported treatment concerns, and was considering stopping to have another baby. This behavior is consistent with other studies (Horne & Weinman, 1999; Horne et al., 1999; Hunot, Horne, Leese, & Churchill, 2007; Neame & Hammond, 2005; Ross et al., 2004). Patients with negative necessity-concerns differential should be considered at greater risk for discontinuing treatment, and should be given continuous information and support.

Treatment concerns included injection issues, side effects, treatment cost, and uncertainty about treatment efficacy. Women's descriptions of injection issues were

consistent with the literature (Harris et al., 2005/2006; Nicholl, 2002). Women switched or discontinued treatment due to injection site reactions. Other concerns voiced were having others inject, fear of needles, and painful injections. It is possible that injection anxiety or fear might be reduced with training, support, and injection equipment (Cox & Stone, 2006). Moreover, reducing injection pain with pharmacological and nonpharmacological strategies may improve injection experiences (Denis et al., 2004).

Side effect profiles reported by the women in this study were also consistent with the literature (Holther & Hohlfield, 1999). Women controlled bothersome side effects through developing strategies and through skipping or switching medications. One woman discontinued after one injection due to intolerance of side effects. Women's side effects decreased over time, similar to other findings (Jacobs, et al., 1996; The IFNB Study Group, 1993; The PRISMS Study Group, 1998). Education and support regarding strategies to minimize or control side effects may be helpful to patients with RRMS.

Cost of the DMDs was not perceived as a barrier to treatment in this study. However, one woman described having to quit her job to be eligible for state-administered insurance, while another woman utilized a drug company's foundation to temporarily subsidize her treatment. Both women expressed uncertainty regarding being able to afford treatment. Insurance issues can represent barriers to treatment for patients. Health care providers may be helpful in advocating for patients with insurance companies or drug company programs.

Uncertainty influenced treatment concerns in this study. Uncertainty was related to unpredictable and bothersome side effects, disease worsening, and questions about treatment efficacy. Four women discontinued use of the injectable DMDs for perceived

lack of active disease or disease worsening while on treatment, consistent with prior studies (Daugherty et al., 2005; Onesti, et al., 2003; O'Rourke & Hutchinson, 2005; Rio, et al., 2005; Ruggieri, et al., 2003; Tremlett & Oger, 2003). Calabresi (2002) suggested that new symptoms may mislead women to confuse treatment side effects with worsening disease. Accurate information and support regarding new symptoms may prevent premature stopping of treatment.

Women's beliefs were fairly evenly divided in their response to "worries about the injectable DMDs" on the BMQ. More specifically, fifty-nine percent of women were worried about the long-term effects of the medications. Although 66% of women indicated that the DMDs "were not a mystery" to them, women's concerns may be related their lack of knowledge about the long-term effects. More long-term studies are needed.

Weighing the Pros and Cons

Women in this study described a process of 'pros and cons', of balancing their perceived treatment benefits against concerns. This finding is congruent with the 'cost-benefit analysis' described in the Beliefs About Medicines framework (Horne and Weinman, 1999). Weighing the 'pros and cons' is a continuous process that begins at initiation of treatment and varies among and within individuals (Johnson et al., 2006). Changes in beliefs due to concrete experiences, information, support, or personal control may influence treatment continuation. Due to the uncertainty of the treatment effects, women in this study who continued to use the injectable DMDs identified hope and fear as motivators for continuing treatment.

Hope and Fear

Women described hope in their treatment and a sense of control not only with, but over, their treatment. Although they were aware that injectable DMDs did not provide a cure, women described hope in reducing symptoms or reducing the number and intensity of relapses. Women also expressed hope for a cure, and for a pill form of treatment.

Fear was expressed by women in terms of uncertainty of the future and consequences of discontinuing the injectable DMDs. Women described not wanting to ‘take a chance’ of stopping treatment for fear that their symptoms or relapses would recur. One woman indicated that her fear of having another serious relapse compelled her to continue her injectable DMD. Therefore, fear was a strong motivator for continuing injectable DMDs. Fear was also expressed regarding injection pain, needle phobia, injection site reactions, and bothersome side effects. Fear and hope were not depicted in the Beliefs About Medicines framework; however these concepts may be unique to complex and difficult treatments, such as injectable DMDs.

These findings are similar to recent studies involving injectable DMDs. Miller and Jezewski (2001) conducted a phenomenological study among patients with RRMS ($N = 20$) who were using interferon beta-1a IM. Patients mentioned having a sense of control with the DMDs to cope with the uncertainty. The experience of managing their injectable DMDs included hope in the DMD as well as hope for a disability-free future. Patients also described fear of needles, injection issues, and cost of treatment. There was no mention of fear of consequences with stopping treatment. Other studies have examined hope and medication use (Fraser, Hadjimichael, & Vollmer, 2001; Fraser, Morgante, Hadjimichael, & Vollmer, 2004; Lindstrom et al., 2006; Verheggen et al.,

1998). Fraser and colleagues (2001) found that hope was significantly related to medication adherence ($p = .03$) in patients with MS who were using injectable DMDs ($N = 341$).

Thorne and colleagues (2004) described “fear points” (p18) experienced by patients throughout their illness course of MS. Patients experienced periods of heightened uncertainty and fear from prediagnosis through postdiagnosis and negotiating the illness. Use of injectable DMDs was not included in that study. Twenty-eight percent of women in this study specifically described continuing treatment out of fear of recurring relapses and disease progression. Yet, many women described fear of needles, injections, and side effects of treatment. The paradox of fear of treatment and fear without treatment has not been well addressed in the literature, and deserves further study.

Johnson and colleagues (2006) conducted a phenomenological study of patients’ perspectives of their injectable DMDs ($N = 18$). Patients described a decision-making process of weighing the pros and cons of treatment. Participants continued with their DMD due to the perceived benefits (fewer relapses, more stable illness course, perceived control); however, they also described concerns related to the treatment, including cost, fear of injections, denial of disease, and uncertainty related to treatment effect). While there was no mention of fear motivating continuing treatment, patients did indicate that they did not want to take a chance of stopping. Those who discontinued or chose not to undergo treatment reported that they did not believe that they were ‘sick enough’; in addition, they attributed non-use of the DMD to fear of side effects, needle phobia, cost, and physician advice. Patients reported that physicians advised them that their illness was ‘stable’ and did not require treatment at that time.

The present study supported Johnson and colleagues' (2006) findings. Patients engage in an ongoing appraisal of their treatment beliefs through concrete experiences, information, and feelings of personal control. The added value of this study is the use of the Beliefs About Medicines framework, which provided a conceptual underpinning for decision-making concerning a complex and difficult treatment.

In summary, the Beliefs About Medicines framework explained women's experiences in this study. The BMQ provided quantitative validation of women's subjective responses. Women's concrete experience with side effects, worsening disease, and lack of disease activity influenced their treatment concerns and adherence behavior. Women weighed the 'pros and cons' of treatment on an ongoing basis. Fear and hope were not explained by the Beliefs About Medicines framework. Fear and hope motivated treatment continuation with injectable DMDs.

Health Care Provider Influence

All of the women in this study were treated by a neurologist or an MS specialist, similar to estimates of MS patients found in the literature (Vickrey et al., 1999). Access to skilled and knowledgeable professionals is essential to patients with RRMS. Patients treated by a neurologist are more likely to be prescribed the most current treatments. Women in this study reported positive attitudes toward their health care providers. Important health care provider characteristics, including expertise in RRMS, attentive listening, information-giving, caring attitude, and openness to shared decision-making were identified.

Attentive listening was described as an important attribute in health care providers. Women reported that 'being heard' by their health care provider was essential.

However, several women described how their health care providers dismissed their concerns regarding new or worsening symptoms. Paterson (2001) found that health care providers minimized or dismissed patients' experiences, leading patients to avoid sharing information or even lie about their health behaviors. This practice can lead to a mistrust and lack of confidence between the health care provider and patient (Thorne et al., 2004).

Uncertainty with RRMS and the injectable DMDs makes it imperative that information is current, relevant, and readily accessible (Thorne et al., 2004). Uncertainty compels information-seeking among patients (Mishel, 1988). Women in this study reported getting most of their information from their health care provider, followed by Internet sites and magazines. All of the women indicated that, although busy, their health care providers were available during health visits and by phone. Women reported that information was effectively explained. Kendrew and colleagues (2001) found that satisfaction with information about medications fostered adherence among patients. Therefore, satisfaction with information regarding injectable DMDs may explain women's adherence to their treatment.

However, some women felt that communication during their health care visit did not include the affect of the illness and treatment on their personal life. Therefore, they felt that they were not given sufficient information and support. Patients have expressed a desire to have information that is tailored to their unique needs (Somerset, Campbell, Sharp, & Peters, 2001). Health care providers need to ask questions that encourage patients to share relevant information regarding the impact RRMS and the injectable DMDs have made on their life (Thorne et al., 2004).

The unique issues related to RRMS and the injectable DMDs require collaborative decision-making during the initial discussion regarding treatment. Uncertainty about the treatment may compel some patients to take an active role in shared decision-making (Heesen et al., 2004; Kasper, Kopke, Mulhauser, & Heesen, 2006). Many women in the study indicated a preference to participate in shared decision-making during initiation of treatment. However, Zwibel (2003) found that patients made treatment decisions alone approximately 40% of the time. Many women said they were given materials to review by their health care provider and told to select a DMD. These women spent extensive time researching treatment choices and were pleased to make their own decision. However, some women preferred to be advised on treatment options. They were concerned that they did not select the most effective treatment. It is important to determine the patients' level of participative decision-making (Denis et al., 2004). In addition, additional time spent providing information specific to each DMD may increase patients' confidence in decisionmaking.

Several women in the study reported discontinuing their injectable DMDs without consulting their health care provider, as described in the literature (Stickel, 2005). Women reported that they discontinued treatment to improve their quality of life. Janse and colleagues (2004) found that differing perceptions of quality of life between patients and health care providers may adversely affect treatment adherence. Health care providers may value injectable DMDs for their (modest) efficacy, while patients may resist treatment due to the bothersome side effects or treatment inefficacy. Approximately one-third of the women reported that the subject of adherence to or problems with injectable DMDs was not addressed during health visits. Thus, ongoing communication is

imperative to discern concerns, questions, or changes in adherence behavior (Bultman & Svarstad, 2000; Denis et al., 2004).

Despite discontinuing their injectable DMDs, most women felt supported by their health care providers. They continued to be monitored with regularly scheduled health visits. One woman reported that her last health visit was several years ago. Her health care provider instructed her to return if she ‘had any problems’. Given the uncertainty of the RRMS illness course, and ongoing subclinical damage, patients who are not experiencing active disease may be misinformed about the importance of regular health visits. Health care providers should reinforce appropriate treatment recommendations, including regular health visits.

Two women in the study were advised not to use injectable DMDs by their health care providers. One woman never started, while another discontinued treatment after a year. This finding is supported in the literature (Holland et al., 2001; Pittock et al., 2006). Some physicians are electing, with their patients, to take a ‘watch and wait’ attitude, and delaying treatment until signs of active disease. This practice runs counter to current treatment guidelines that recommend immediate and sustained treatment for all patients with RRMS. Uncertainty regarding adherence to treatment guidelines can lead to confusion and increased anxiety for the patient. Health care providers must provide timely and accurate information, monitoring, and support to ensure optimal treatment for these patients.

The presence of fear and hope in women who are continuing their treatment should be explored by health care providers. Women maintain a continual process of weighing the pros and cons of their injectable DMDs; yet, many times they deliberately

ignore, control, or tolerate bothersome treatment effects because of their beliefs in treatment necessity. Fear of treatment and fear without treatment constitute a powerful paradox for patients. Women in this study described how they refrained from asking questions or sharing information at their health care visits. Thorne and colleagues (2004) found that communication that was ongoing, accurate, up-to-date, and patient-centered, help patients manage fear related to their MS. Conversely, insufficient or withheld information, technical jargon, delayed appointments and lack of empathy heightens fear and uncertainty in patients. It is conceivable that health care communication that focuses on patients' experiences, beliefs, concerns, hopes, and fears concerning the injectable DMDs may foster better understanding and improved collaboration among patients and health care providers in managing RRMS.

In summary, information and support are essential for patients who are managing their RRMS and injectable DMDs. Furthermore, attentive listening and discerning relevant psychosocial information may assist health care providers to meet the unique needs of patients. Collaborative decision-making during initiation and ongoing treatment may ensure understanding of patients' changing symptom experience or beliefs that hamper adherence. Finally, clarity about treatment guidelines, including regular health visits, may improve patients' management of their RRMS, and improve quality of life.

Limitations

There are several limitations in this study. First, this is a cross-sectional study, using a one-time interview to explore adherence behaviors and beliefs among women with RRMS who are using injectable DMDs. The small sample size limits generalizability to the larger population of women with RRMS who are using injectable

DMDs. The majority of participants in this study were recruited from a central Massachusetts MS clinic or neurology practice. Their experiences may not reflect experiences of women who are treated by general practice physician or in other areas. Further, women self-selected to participate in this study. They may not share the same experience as women who chose not to participate. Finally, the order of data collection may have influenced women's responses. Women were interviewed with qualitative questions first, followed by the BMQ instrument. The interview questions related to women's beliefs may have influenced women's responses on the BMQ.

Implications for Research

This study added knowledge regarding women's parallel experiences of managing RRMS and injectable DMDs, including adherence behaviors, women's beliefs about the DMDs, and health care provider influence on illness and treatment management. Further study is appropriate in several areas. A study of women's adherence behaviors and beliefs over time is needed to anticipate factors that may adversely affect management of injectable DMDs. In addition, expanded use of the BMQ among a larger sample of participants is necessary to validate the preliminary findings in this study. A study of men's experiences and beliefs regarding injectable DMDs is important, as their perspective may differ from women. Finally, a study on the effect of communication techniques on patients' adherence to the injectable DMDs may improve health care provider-patient relationships, and result in better management of RRMS.

Implications for Practice

The findings in this study identify communication as a powerful tool in managing uncertainty among patients with RRMS. Health care providers must give patients

ongoing, accurate, and timely information; in addition, health care providers must discern the psychosocial as well as the physical and emotional impact of RRMS and the injectable DMDs. Women in this study continued with their injectable DMDs despite barriers to treatment. However, they exhibited uncertainty regarding treatment benefit as well as concerns about the long-term effects of the DMDs. Health care providers must assess patients' concrete experience and beliefs at every health care visit in order to provide relevant and patient-specific information and support.

Nurses play an integral role in educating and supporting patients as they manage their RRMS. Nurses spend time with patients within and between visits. Information and support through in-person and telephone counseling by nurses can help patients to manage uncertainty, share concerns, and identify barriers to treatment. Nurses can also refer patients to resources that increase their knowledge and understanding about RRMS and injectable DMDs. Finally, by evaluating the psychosocial impact of RRMS and injectable DMDs on patients' lives, nurses can implement more patient-centered interventions that may improve management of RRMS and injectable DMDs.

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Table 1. Types and Prevalence of MS

Relapsing-Remitting (RRMS) (85%) — acute, self-limited episodes of neurologic dysfunction that develop over days and weeks, with partial or complete recovery over weeks to months.
<p>Secondary-Progressive (SPMS) — begins as RRMS; as disease progresses, relapses decline and are replaced by slow, steady progression.</p> <p>50% with RRMS have SPMS in 10 years; 90% with RRMS have SPMS in 25 years.</p>
Primary-Progressive (PPMS) (10%) — Gradual, steady deterioration without superimposed relapses.
Progressive-Relapsing (5%) — Continuous disease progression with occasional superimposed relapses.
Source: Lublin, F.D. & Reingold, S.C. (1996). <i>Neurology</i> , 46, 907-911.

Table 2. Kurtzke Disability Status Scale

0.0= Normal neurological exam;
1.0= No disability, minimal signs in one (Function system) (FS)*;
1.5= No disability, minimal signs in more than one FS;
2.0= Minimal disability in one FS;
2.5= Minimal disability in more than one FS;
3.0= Fully ambulatory; moderate disability in one FS, or moderate disability in 3-4 FS;
3.5= Fully ambulatory; moderate disability in one FS;
4.0= Fully ambulatory; self-sufficient; up and about 12 hours even with severe disability; able to walk 500 meters without aid or rest;
4.5= Fully ambulatory; self-sufficient; may require minimal assistance; relatively severe severe disability; able to walk 300 meters without aid or rest;
5.0= Ambulatory to 200 meters without aid or rest; disability severe enough to impair daily activities (e.g., work);
5.5= Ambulatory to 100 meters without aid or rest; disability severe enough to preclude full daily activities;
6.0= Intermittent or unilateral constant assistance (cane, crutch, or braces) required to walk 20 meters without resting;
6.5= Constant bilateral assistance (cane, crutches, brace) required to walk 100 meters with or without resting;
7.0= Unable to walk beyond 5 meters even with aid; essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up in wheelchair 12 hours a day;
7.5= Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but carry on in a standard wheelchair a full day; may require a motorized wheelchair;
8.0= Essentially restricted to bed or chair or perambulated in wheelchair; but may be out of bed much of the day; retains many self-care functions; generally has effective use of arms;
8.5= Essentially restricted to be much of the day; has some effective use of arm(s); retains some self-care functions;
9.0= Helpless bed patient; can communicate and eat;
9.5= Totally helpless bed patient; unable to communicate effectively or eat/swallow;
10.0= Death due to MS.

Source: Kurtzke, J.F. (1983). *Neurology*, 33, 1444-1452.

Note: Functional Systems (FS) are eight scales representing different functions of the CNS (Kurtzke, 1961). Each system is rated on a five-point (three systems) or six-point (four systems) response scales except 'Other Functions' which is rated dichotomously (0=none, 1=any other neurological findings attributed to multiple sclerosis).

Table 3. Immunomodulatory Agents for RRMS

Type	Interferon Beta-1a IM (Avonex)	Interferon Beta-1a SC (Rebif)	Interferon Beta-1b SC (Betaseron)	Glatiramer Acetate (Copaxone)
Manufacturer	Biogen	Ares-Serono	Berlex	Teva Marion Partners
Approved in US	1996		1993	1996
Cost* (Wholesale)	\$16,608	\$20,553	\$17, 827	\$16,026
Dosage; route; Frequency	30 mcg (6MIU) IM/ Weekly	22 or 44 mcg (6 or 12 MIU) SC/ 3 times/week	250 mcg (8MIU) SC/ Every other day	20 mg SC/ Daily
Common Side Effects+	Increased depression, suicidal ideation, new or worsening psychiatric disorders; flu-like symptom complex; headache; paresthesia; hypertonia; myasthenia; pain; myalgia	Increased depression, suicidal ideation, suicide attempts, new or worsening psychiatric disorders; flu-like symptom complex; headache; injection-site reaction; abnormal liver function tests; leukopenia; myalgia; back pain	Use with caution with depression; flu-like symptom complex; lymphopenia; injection-site reactions; asthenia; hypertonia; headache; pain; injection-site necrosis (5%);	Injection site reactions; vasodilatation; chest pain; asthenia; infection; pain; nausea; arthralgia; anxiety; hypertonia; Post-injection pseudo-anaphylaxis symptom complex (10%)

*Source: National Multiple Sclerosis Society. Available at: <http://www.nationalmssociety.org/Research-TysabriQ&A.asp>.

+ Source:

Avonex: Data on file. Biogen IDEC, 2005. Available at <http://www.avonex.com>.

Rebif: Data on file. Serono, Inc. 2004. Available at <http://www.rebif.com>.

Betaseron: Data on file. Berlex Laboratories, 2003. Available at http://www.berlex.com/html/products/pi/Betaseron_Medication_Guide.pdf.

Copaxone: Data on file. Teva Neuroscience, 2004. Available at http://www.mswatch.com/ContentRoot/miscellaneous/pdfs/PI_Copp0204HW_Oct04.pdf.

Table 4. Efficacy Profiles Demonstrated by Phase III, 2-year Clinical Trials

Type	IFNB-1a IM Avonex	IFNB-1a SC Rebif	IFNB-1b Betaseron	Glatiramer Acetate Copaxone
Phase III Study	Jacobs et al, 1996	PRISMS Study Group, 1998	The IFNB MS Group, 1993	Johnson et al, 1995
Pt. Population (med; placebo)	N=301; (158; 143)	N=560 (189/184; 187)	N=372 (125/124; 123)	N=251 (125;126)
Dosage	30 mcg IM weekly (n=158)	22mcg 3x/week (n=189); 44 mcg 3x/week (n=184)	1.6 MIU every other day (n=125); 8MIU every other day (n=124)	30 mg every day (n=125)
Endpoints	Primary: 8 Secondary: 1,2,4,6, 9	Primary: 9, 10 Secondary: 2-4, 6,8	Primary: 1,2 Secondary: 3-7	
Reduced Relapse Rate*	32% (p= .002)	27% (22 mcg) (p< .005); 33% (44 mcg) (p< .005)	34% (8MIU) (p= .0001)	29% (p= .007)
Sustained Disability*	37% (p=.02)	22% (22 mcg) (p= .04); 30% (44 mcg) (p= .01)	29% (NS)	No difference
Decreased number Gd + lesions**	89% (2y) (p= .003)	84% (2y) (p< .0001)	83% (p=.0089)	29% (9 mo) (p= .003)
Decrease in T2 lesions	91% (18 mo) (p= .001)	67% (22 mcg) 78% (44 mcg) (p< .0001)	75% (2y) (p= .0026)	30% (9 mo) (p= .003)
Decrease in T1 black holes***	68% (2y) (NS)	No data	No data	37% (9 mo) (NS)
Decrease in brain atrophy	55% (2y) (p= .03)	No data	No data	2.5% (18 mo) (p= .037)

Note: Endpoints:

1=annual exacerbation rate

2=proportion of relapse-free patients

3=number of patients who progressed at 2 years

4=median time to first relapse

5 =exacerbation duration and severity

6=mean annual change in EDSS

7=median time to progression

8=mean time to progression

9=number of relapses per patient

10=relapse severity

Note: Results are as compared to placebo-group.Total over 2 years. ** Gd+ lesions—gadolinium-positive lesions. ***T1 black holes represent axonal loss and demyelination.

Table 5. Treatment Recommendations of the Medical Advisory Board of the NMSS on the Use of IFNB-1a IM, IFNB-1a SC, IFNB-1b, and Glatiramer Acetate

- Initiation of therapy is advised as soon as possible following a definite diagnosis of MS with active disease, and may also be considered for selected patients with a first attack who are at high risk of MS
- Patients' access to medication should not be limited by the frequency of relapses, age, or level of disability
- Treatment is not to be stopped during evaluation for continuing treatment
- Therapy is to be continued indefinitely except for the following circumstances: there is a clear lack of benefit; there are intolerable side effects; better therapy becomes available.
- All of the FDA-approved agents should be included in formularies and covered by third party payers so that physicians and patients may determine the most appropriate agent on an individual basis—failure to do so is unethical and discriminatory
- Movement from one immunomodulator drug to another should occur only for medically appropriate reasons
- Immunosuppressant therapy with Novantrone © (mitoxantrone) may be considered for selected relapsing patients with worsening disease or patients with secondary-progressive multiple sclerosis
- Most concurrent medical conditions do not contraindicate use of the immunomodulatory drugs
- None of these therapies has been approved for use by women who are trying to become pregnant, are pregnant, or are nursing mothers

Source: National MS Society. Available at:
http://www.nationalmssociety.org/docs/HOM/EXP_Consensus.pdf

Table 6. Most common side effects related to the DMDs

	IFNB-1b (25 mg)	IFNB-1a IM (30mcg)	IFNB-1bSC (44 mcg)	Glatiremar Acetate (20mg)
Injection site reactions	85%	8%	92%	73%
Headache	57%	58%	70%	5%
Flu-like symptoms	60%	49%	59%	19%
Pain	51%	23%	---	---
Fatigue	---	---	41%	---
Myalgia	27%	29%	25%	---
Fever	36%	25%	28%	8%
Depression	34%	18%	---	---
Palpitations		---	---	17%
Chest pain		---	---	21%
Dyspnea		---	---	19%
Lymphocyte abnormality	88%	---	---	---

Source: Data on file (Berlex laboratories, 2003; Biogen Inc, 2003; Serono Inc, 2004; Teva Neuroscience, 2004)

Table 7. Conceptual definitions from the Beliefs About Medicines Framework

Concept	Definition	Operational definition
Treatment Necessity	Belief that a particular medicine is necessary for treatment	Belief About Medicines Questionnaire Qualitative Interview: - Subjective Experiences -Symptom Experience - Benefits of Immunomodulators - Illness representation - Health Care Provider Influence
Perceived Concerns	Anticipations of unpleasant side effects or disruptions by a particular medication	-Beliefs About Medicines Questionnaire Qualitative Interview: -Subjective experiences -Barriers: -adverse effects -finances -injection issues -lack of efficacy -intrusiveness -Health Care Provider influence
Necessity-Concerns Differential	The balance between treatment necessity and specific concerns about the prescribed medicine, determined using a cost-benefit appraisal	Beliefs About Medicines Questionnaire: calculated difference between treatment necessity and perceived concerns.

Source: Horne, R. (1997). Representations of medication and treatment: Advances in theory and measurement. In K.J. Petrie & J. A. Weinman, *Perceptions of health & illness*. The Netherlands: Harwood Academic Publishers, 155-188.

Table 8: Demographic Characteristics of the Sample

Demographic	Mean	Range	SD
Age	47	32-66 years	7.35
Time with RRMS (Months)	99	8-348 months	96.7
Time on IIM Treatment (months)	37	4-132 months	30.5

Table 9: Types and usage of Injectable DMDs

DMD	Frequency (<i>n</i>)	Percentage
IFNB-1a IM (Avonex)	15	60
Glatiremar acetate (Copaxone)	6	24
IFNB-1b (Betaseron)	2	8
IFNB-1a SQ (Rebif)	2	8

Table 10. Symptoms Reported by Participants

Symptoms	Frequency (<i>n</i>)	Percentage
Fatigue	16	50%
Difficulty walking	14	44%
Cognitive issues	13	41%
Numbness	11	34%
Weakness	7	22%
Vision problems	7	22%
Leg pains/spasms	6	19%
Tingling	6	19%

Table 11. Symptoms of RRMS and Strategies

Symptom	Strategies
Fatigue	Nap, relax, rest, 'take down time', 'push through the fatigue', 'slow down', change work habit, avoid warm weather, ask for help
Walking difficulty	Don't walk long, monitor legs, 'wait for feet', use support (carriage), don't walk alone, play indoors with grandchildren, stop aerobics, start exercise
Cognitive issues	Write things down, re-read information multiple times
Numbness	Avoid very warm water, minimize stress

Table 12. Common Injectable DMDs Issues and Strategies

IIM issues	Strategies
Planning	Calendar, schedule
Rotating sites	Create a grid of sites, Leave bandaid on the last site
Injection pain	Ice, EMLA (anesthetizing cream) Analgesics (acetaminophen, ibuprophen)
Injection site lumps	Ice, rotate sites
Injection site itchiness	Cortisone cream
Injection phobia	Have others inject, Inject slowly, quiet place
Travel	Get supplies, guidance from IIM company
Flu-like side effects	Inject at night, acetaminophen, ibuprophen, Schedule sufficient rest, hydration
Severe side effects	Avoid arms, use buttocks

Table 13. Results from the Beliefs About Medicines Questionnaire

Belief	Mean	Median	SD
Present health depends on injectable DMD	3.06	3.00	1.29
Life impossible without injectable DMD	2.19	2.00	1.15
Very ill without injectable DMD	2.78	3.00	1.16
Future health depends on injectable DMD	3.44	4.00	1.19
Injectable DMD protects from getting worse	4.00	4.00	1.14
Worries about using injectable DMD	2.88	2.00	1.48
Worries about long term effects of injectable DMD	3.38	4.00	1.41
Injectable DMD is a mystery	2.50	2.00	1.02
Injectable DMD disrupts life	2.13	2.00	1.34
Worries about becoming dependent on the injectable DMD	1.66	1.50	1.50

Note: Statements were on a 5-point Likert scale; 1= strongly disagree; 5= strongly agree.

Table 14. Necessity-Differential Scores.

Participant ID	Tx Status	Necessity-Differentials Score
1	On Tx	-5
2	On Tx	+1
3	On Tx	-9
4	On Tx	+6
5	On Tx	+8
6	On Tx	+5
7	On Tx	+1
8	On Tx	+12
9	On Tx	+6
10	On Tx	+7
11	On Tx	+9
12	On Tx	-4
13	On Tx	+5
14	On Tx	+13
15	On Tx	+1
16	On Tx	+14

Participant ID	Tx Status	Necessity-Differentials Score
17	On Tx	+9
18	On Tx	+6
19	Off Tx	-8
20	On Tx	+6
21	On Tx	+5
22	On Tx	+3
23	Off Tx	-14
24	On Tx	+2
25	Never on Tx	-5
26	Off Tx	-13
27	On Tx	+4
28	On Tx	+5
29	Off Tx	-7
30	On Tx	+11
31	On Tx	+8
32	On Tx	+12

Note: *Status on Treatment*: On treatment (on Tx); Off treatment (off Tx); never on treatment (never on Tx).
Necessity Differentials-score: positive scores signify greater necessity beliefs; negative scores signify greater concerns.
Bolded row indicates negative score for a woman on treatment.

Table 15. Pros and Cons related to the injectable DMDs

Pros	<i>n</i>	Percent	Cons	<i>n</i>	Percent
Doesn't want to get worse	8	32%	Side Effects	9	36%
No side effects	6	24%	Uncertainty	7	28%
Hope	6	24%	Hates needles	5	20%
No relapses	5	20%	Injection site reactions	5	20%
Mild or no SE	5	20%	Painful injections	5	20%

Appendix A. *Qualitative Interview Guide (Users)*

Subject # _____

Date _____

Conceptual Area	Interview Question	Probes
I. Subjective experience of day-to-day management with injectable immunomodulators	Can you tell me your story related to RRMS?	How has your life changed since you were diagnosed with RRMS?
	Can you tell me what it's like for you to use the injectable immunomodulator?	a) Tell me about any special routine you have concerning your injection? b) Have you made any changes over the last month with your injection routine? c) What factors (if any) have made it easy for you to manage your injectable DMD?
Ia. Perceived Barriers	Is there anything that makes it hard for you to use or continue your injections?	a) Do you have any problems giving yourself the injection? b) Have any side effects made it hard for you to use or continue your injections? c) Have insurance or money issues made it hard for you to use or continue your injections?
Ib. Adherence issues	What is your experience with missed or skipped doses of the injectable immunomodulator?	a) Some people have told me that they sometimes skip their injection, forget to take it, or change the dose. Has anything like this happened to you? b) Some people have told me that they sometimes stop taking their injection for a while. Has anything like this happened to you?
IIa. Treatment Necessity	How have things changed since you started the injections?	a) Since you started your injections, do you think your RRMS has improved?

		<p>Worsened? Remained the same?</p> <p>b) What do you see as the greatest benefits of the injection?</p> <p>c) What have you been told about the benefits of the injection medication?</p> <p>d) What do you think would happen if you weren't using the injection medication?</p>
IIb. Specific Concerns	What concerns you about the injections?	<p>a) What have you been told about the negative aspects of the injections?</p> <p>b) Some people have said that the injections have disrupted their lives. Has anything like that happened to you?</p> <p>c) What have you done about your concerns?</p> <p>d) Have you thought about your long-term plans with the injection medication?</p>
IV. Health Care Provider influence on injectable immunomodulator day-to-day management	How do your doctors and nurses influence how you manage your injection medication?	<p>a) What was your discussion with the HCP like when you decided to start the injection therapy?</p> <p>b) Do you feel you spend enough time talking about the injectable medication during your visit?</p> <p>c) Have you ever called your HCP when you have had problems with your therapy?</p> <p>d) Have you ever discussed stopping therapy or 'taking a break' from therapy with your HCP?</p> <p>e) What advice would you give HCPs about helping patients like yourself to manage the injection medication?</p>

Appendix B. *Qualitative Interview Guide (Discontinued use)*

Subject # _____

Date _____

Conceptual Area	Interview Question	Probes
I. Subjective experience of day-to-day management without injectable immunomodulators	Can you tell me your story related to RRMS?	How has your life changed since you were diagnosed with RRMS?
Ia. Perceived Barriers	What made it hard for you to continue your injections?	a) Did you have any problems giving yourself the injection? c) Did any side effects make it hard for you to use or continue your injections? e) Have insurance or money issues made it hard for you to use or continue your injections?
Ib. Adherence issues	Prior to stopping, what was your experience with missed or skipped doses of the injection?	a) Some people have told me that they sometimes forget to take their injection. Did anything like that happen to you? b) Some people have told me that they sometimes skip their injection or change the dose. Did anything like this happen to you? c) Some people have told me that they sometimes stop taking their injection for a while. Did anything like this happen to you?
Ila. Treatment Necessity	How did things change when you started the injections? How have things changed since you stopped the medication?	a) Since you started your injections, did you think your RRMS had improved? Worsened? Remained the same? b) What did you see as the greatest benefits of the injection? c) What were you told about

		<p>the benefits of the injection medication?</p> <p>d) Do you think anything is different because you aren't using the injectable immunomodulators?</p>
IIb. Specific Concerns	What concerned you about the injection?	<p>a) What do you know about the negative aspects of the injections?</p> <p>b) Some people have said that the injections have disrupted their lives. Did anything like that happen to you?</p> <p>c) What did you do about your concerns?</p> <p>d) Have you thought about your long-term plans with your medication decisions?</p>
IV. Health Care Provider influence on injectable immunomodulator day-to-day management	How did your doctors and nurses influence how you managed your injection medication?	<p>a) What was your discussion with the HCP like when you were deciding whether to start the injection therapy?</p> <p>b) Did you spend any time talking about the injectable medication during your visits?</p> <p>c) Did you ever call your HCP when you had problems with your therapy?</p> <p>d) Did you ever discuss stopping therapy or 'taking a break' from therapy with your HCP?</p> <p>e) What advice would you give HCPs about helping patients like yourself to manage the injection medication?</p>

Appendix C. *Qualitative Interview Guide (Never used)*

Conceptual Area	Interview Question	Probes
I. Subjective experience of day-to-day management without injectable immunomodulators	Can you tell me your story related to RRMS?	a) How has your life changed since you were diagnosed with RRMS? b) Have you had any changes in your RRMS over the last year? c) How did you come to the decision not to start the injectable medications?
Ia. Perceived Barriers	Is there anything that has made it hard for you to begin to use injectable medications?	a) Have insurance or money issues made it hard for you to start using injections? b) Have family issues made it hard for you to start using injections?
Ila. Treatment Necessity	What do you think are the benefits to the injectable medications?	a) What do you know about the benefits of the injectable medications? b) Where do you/have you gotten information about the injectable medications? b) Do you think anything is different with your RRMS because you aren't using the injectable medications?
Ilb. Specific Concerns	What concerned you about the injectable medications?	a) What concerns you about the injectable medications? b) What have you been told about the negative aspects of the injections? c) What did/have you done about your concerns? d) Have you thought about your long-term plans with your medication decisions?
IV. Health Care Provider	How do (have) your doctors	a) What was your

influence on injectable immunomodulator day-to-day management	and nurses influence(d) your decision regarding injectable medication?	discussion with the HCP like when you were deciding whether to start the injection therapy? b) Did/do you feel you spend enough time talking about the injectable medication during your visit? b) What advice would you give HCPs about helping patients like yourself to manage the injectable medication?
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Appendix D. *Demographic Data Sheet*

Subject # _____

Date _____

The following information will be collected during patient interview:

1. Age at last birthday: _____ years

2. Gender

Male _____ ()1

Female _____ ()2

3. Race/ethnicity:

___ Caucasian/White _____ ()1

___ African American _____ ()2

___ Hispanic _____ ()3

___ Asian American _____ ()4

___ Native American _____ ()5

___ Other _____ ()6

If other, please specify _____

4. Marital Status:

___ Married _____ ()1

___ Widowed _____ ()2

___ Single _____ ()3

___ Separated _____ ()4

___ Divorced _____ ()5

Subject # _____
Date _____

____ Living with Partner ____ ()6

____ Other ____ ()7

____ If other, please specify: ____

5. Occupation:

____ Working full-time ____ ()1

____ Working part-time ____ ()2

____ On leave from work ____ ()3

____ On disability ____ ()4

____ Retired ____ ()5

____ Student ____ ()6

____ Other ____ ()7

____ If other, please specify: ____

Subject # _____
Date _____

6. Insurance Status:

____ Private _____ ()1

____ Medicare _____ ()2

____ Medicaid _____ ()3

____ No insurance _____ ()4

____ Don't know/

____ Don't remember _____ ()5

____ Other _____ ()6

____ If other, please specify: _____

7. Education:

____ # Years completed: _____

____ Don't know/

____ Don't remember _____ ()1

8. Diagnosis of RRMS:

____ # Years with RRMS: _____

____ Don't Know/

____ Don't remember _____ ()1

Subject # _____
Date _____

9. Worsening Disease:

_____ # Relapses over the last year: _____

_____ Don't know _____

_____ Don't remember _____ ()1

10. Immunomodulator Treatment

_____ # Years on injectable Rx: _____

_____ Don't Know/ _____

_____ Don't remember _____ ()1

11. Type of injectable Rx currently

_____ using: _____

_____ Avonex _____ ()1

_____ Rebif _____ ()2

_____ Betaseron _____ ()3

_____ Copaxone _____ ()4

_____ None _____ ()5

Subject # _____
Date _____

12. Types of injectable Rx used

_____ before: (List all)

_____ Avonex _____ ()1

_____ Rebif _____ ()2

_____ Betaseron _____ ()3

_____ Copaxone _____ ()4

_____ None _____ ()5

_____ Don't know/

_____ Don't remember _____ ()6

13. Adherence: In the past month,

how often did you miss your

MS medication?

_____ Did not miss any doses _____ ()1

_____ Missed one or more doses()2

_____ Don't know/

_____ Don't remember _____ ()3

Subject # _____
Date _____

14. Where do you go for information
about your illness (RRMS)
and/or injectable medication?
(Please rank in order of
preference)

____ Health care provider/
(MD, NP, PA) _____ ()1

____ Health care staff/
(RN, LPN) _____ ()2

____ Books, pamphlets,
Magazines _____ ()3

____ Websites _____ ()4

____ Support groups _____ ()5

____ Others with RRMS _____ ()6

____ Other _____ ()7

____ If other, please explain _____

Appendix E. *Beliefs About Medicines Questionnaire*

Subject # _____

Date _____

Scale:

- (1) Strongly Disagree
- (2) Disagree
- (3) Uncertain
- (4) Agree
- (5) Strongly Agree

BMQ—Specific Necessity

- _____ 1. My health, at present, depends on my injectable medicine.
- _____ 2. My life would be impossible without my injectable medicine.
- _____ 3. Without my medicines I would be very ill.
- _____ 4. My health in the future depends on my injectable medicine.
- _____ 5. My injectable medicine protects me from becoming worse.

BMQ—Specific Concerns

- _____ 1. Having to take the injectable medication worries me.
- _____ 2. I sometimes worry about long-term effects of my medicines.
- _____ 3. My injectable medicine is a mystery to me.
- _____ 4. My injectable medicine disrupts my life.
- _____ 5. I sometimes worry about becoming dependent on my injectable medicine.